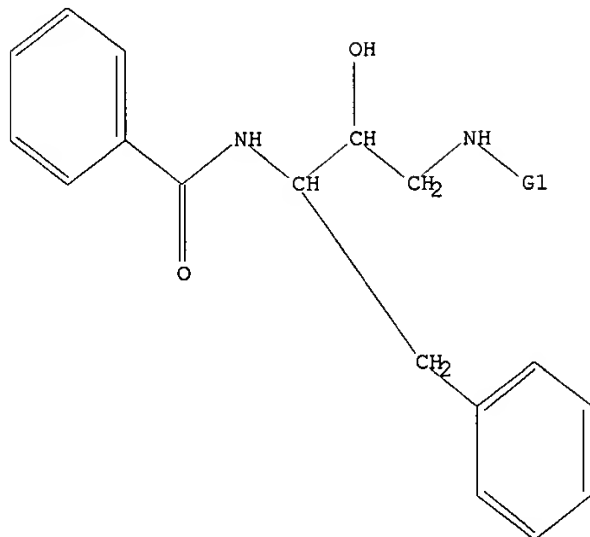


09/288,556

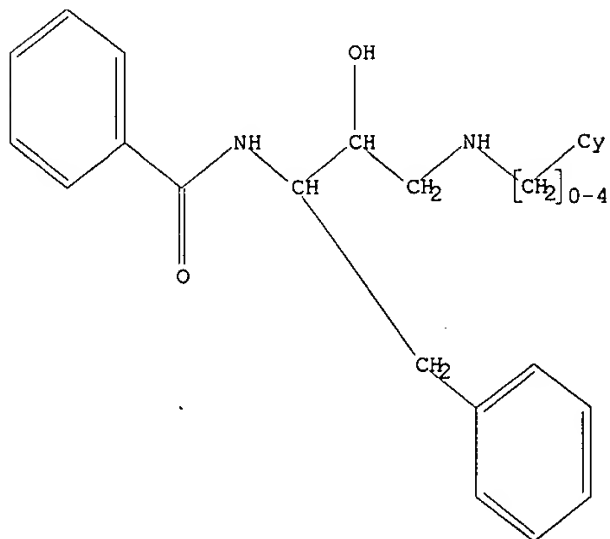
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L1 STR



G1 n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu

Structure attributes must be viewed using STN Express query preparation.

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L2 HAS NO ANSWERS  
L2 STR



Structure attributes must be viewed using STN Express query preparation.

09/288,556

=> s l1 sss full

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FULL SCREEN SEARCH COMPLETED - 13077 TO ITERATE

100.0% PROCESSED 13077 ITERATIONS  
SEARCH TIME: 00.00.01

10 ANSWERS

L3 10 SEA SSS FUL L1

=> s l2 sss full

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FULL SCREEN SEARCH COMPLETED - 13071 TO ITERATE

100.0% PROCESSED 13071 ITERATIONS  
SEARCH TIME: 00.00.01

1545 ANSWERS

L4 1545 SEA SSS FUL L2

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

310.84

311.05

FILE 'CAPLUS' ENTERED AT 10:17:00 ON 22 MAR 2004  
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE COVERS 1907 - 22 Mar 2004 VOL 140 ISS 13  
FILE LAST UPDATED: 21 Mar 2004 (20040321/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L5 4 L3

=> s l4

L6 13 L4

09/288,556

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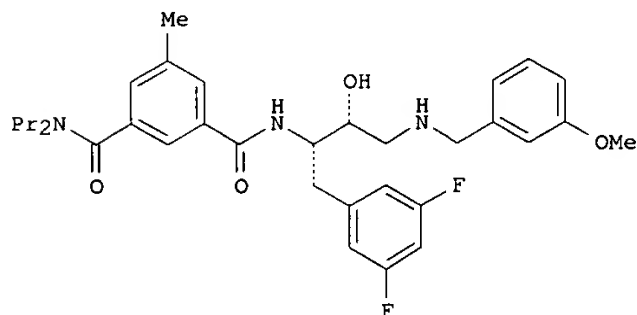
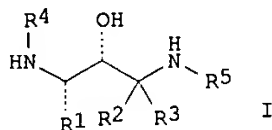
L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:696859 CAPLUS  
DOCUMENT NUMBER: 139:230480  
TITLE: Preparation of substituted amines prodrugs useful in  
treating Alzheimer's disease  
INVENTOR(S): Varghese, John; Jagodzinska, Barbara; Maillard,  
Michel; Beck, James P.; Tenbrink, Ruth E.; Getman,  
Daniel  
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn  
SOURCE: PCT Int. Appl., 483 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072535	A2	20030904	WO 2003-US7287	20030227
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2002-359953P P 20020227

OTHER SOURCE(S): MARPAT 139:230480

GI



II

AB Amines (I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.; e.g. N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide], useful in treating Alzheimer's disease and other similar diseases, were prepared. Although the methods of preparation are not claimed, hundreds of example preps. are included. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamic acid in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II (N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide). The compds. I exhibit an IC50 of < 50  $\mu$ M against  $\beta$ -secretase.

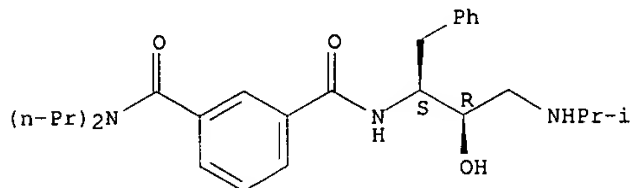
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RN **388062-20-2** CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

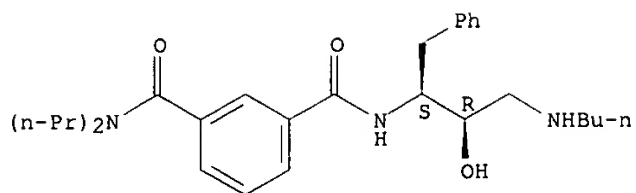


RN **388062-33-7** CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

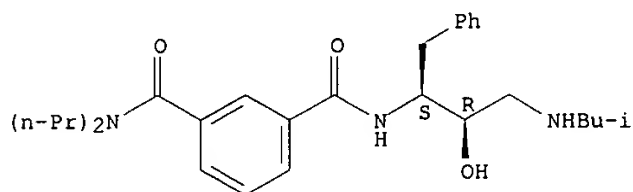
09/288,556



RN 388062-99-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

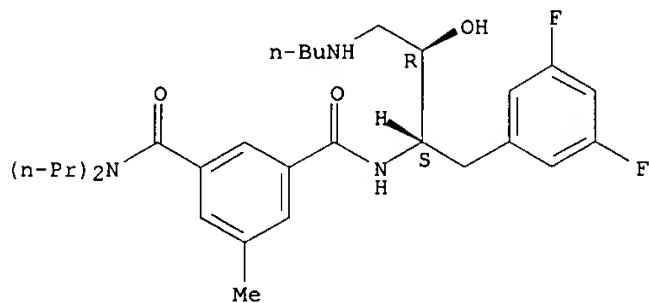
Absolute stereochemistry.



RN 388063-39-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

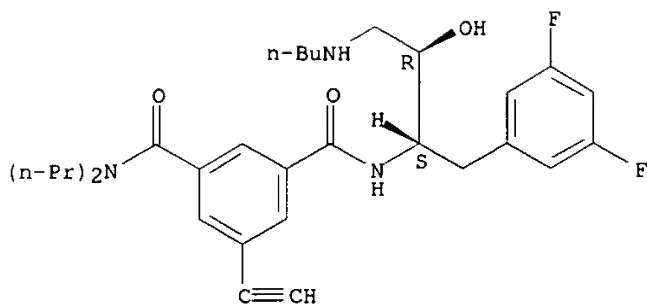


RN 388065-53-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-ethynyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

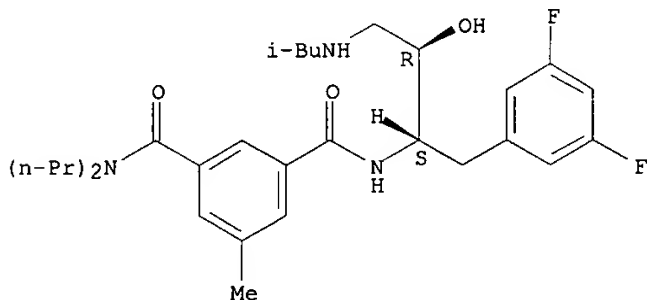
09/288,556



RN 590423-35-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'--[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:412801 CAPLUS

DOCUMENT NUMBER: 139:245782

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 1243 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

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WO 2003040096 A2 20030515 WO 2002-US36072 20021108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
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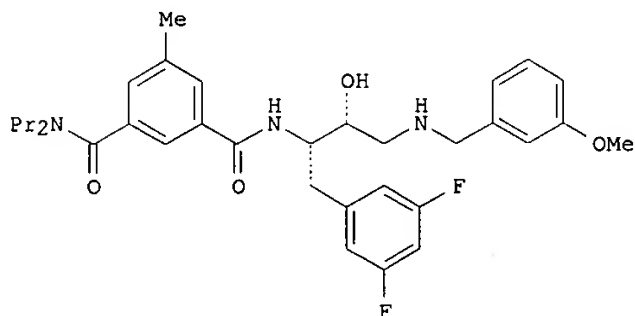
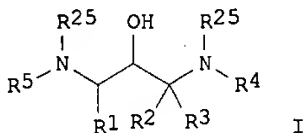
PRIORITY APPLN. INFO.:

US 2001-337122P P 20011108  
 US 2001-344086P P 20011228  
 US 2002-345635P P 20020103  
 WO 2002-US36072 A 20021108

OTHER SOURCE(S):

MARPAT 139:245782

GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO<sub>2</sub>, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO<sub>2</sub>, (un)substituted CH<sub>2</sub>; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy,

etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared. E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC<sub>50</sub> of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.

IT 597559-81-4P

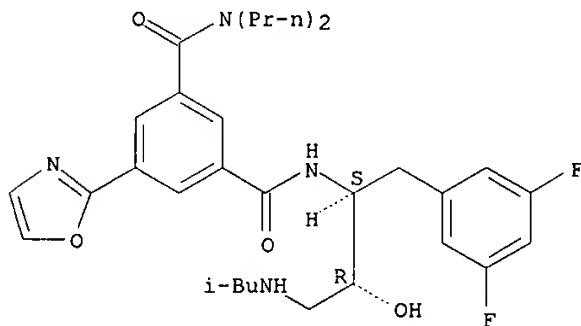
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 597559-81-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-5-(2-oxazolyl)-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:376819 CAPLUS

DOCUMENT NUMBER: 138:385173

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 1243 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

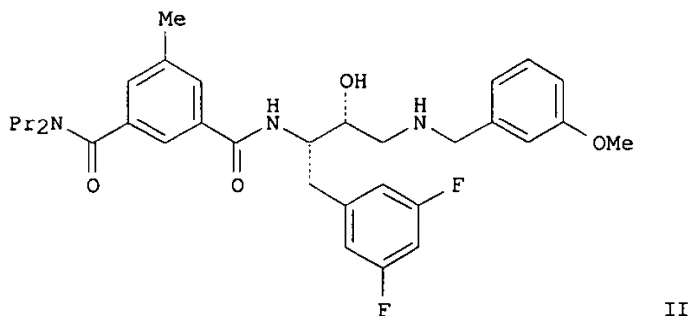
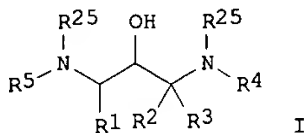
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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NE, SN, TD, TG  
WO 2003040096 A2 20030515 WO 2002-XA36072 20021108  
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NE, SN, TD, TG  
PRIORITY APPLN. INFO.: US 2001-337122P P 20011108  
US 2001-344086P P 20011228  
US 2002-345635P P 20020103  
WO 2002-US36072 A 20021108  
OTHER SOURCE(S): MARPAT 138:385173  
GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un)substituted CH2; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy,

etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared. E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC<sub>50</sub> of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 527718-24-7P 527726-59-6P 527727-51-1P

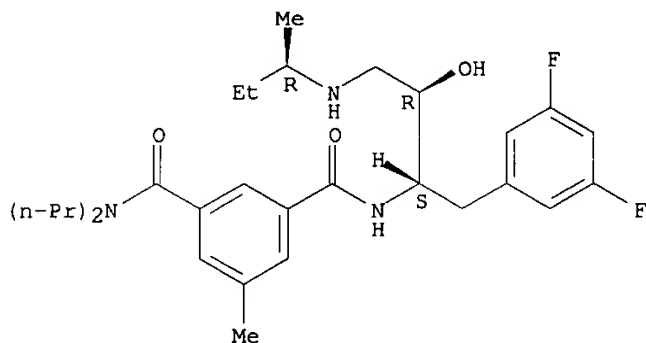
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 527718-24-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(1R)-1-methylpropyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

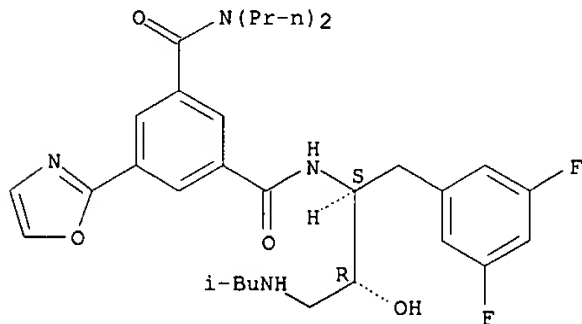
Absolute stereochemistry.



RN 527726-59-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(2-methylpropyl)amino]propyl]-5-(2-oxazolyl)-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

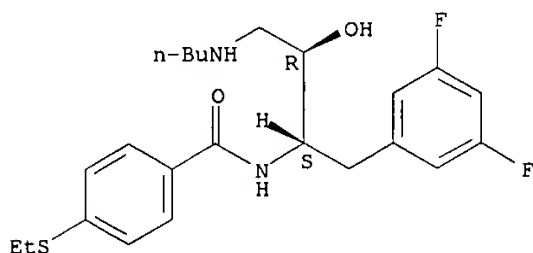


HCl

RN 527727-51-1 CAPLUS

CN Benzamide, N-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-4-(ethylthio)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:31402 CAPLUS

DOCUMENT NUMBER: 136:102190

TITLE: Preparation of substituted amines to treat Alzheimer's disease

INVENTOR(S): Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia &amp; Upjohn Company

SOURCE: PCT Int. Appl., 651 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

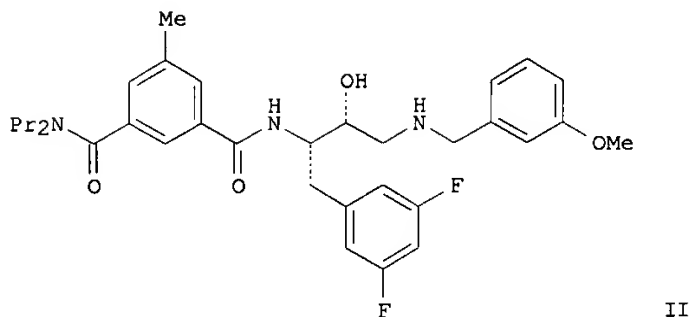
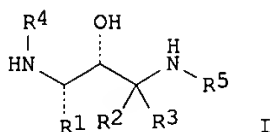
FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002512	A2	20020110	WO 2001-US21012	20010629
WO 2002002512	A3	20030821		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002128255	A1	20020912	US 2001-896139	20010629
BR 2001012000	A	20030603	BR 2001-12000	20010629
EP 1353898	A2	20031022	EP 2001-952378	20010629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502669	T2	20040129	JP 2002-507769	20010629
NO 2002006199	A	20030221	NO 2002-6199	20021223
PRIORITY APPLN. INFO.:				
			US 2000-215323P	P 20000630
			US 2000-252736P	P 20001122

US 2000-255956P P 20001215  
 US 2001-268497P P 20010213  
 US 2001-279779P P 20010329  
 US 2001-295589P P 20010604  
 WO 2001-US21012 W 20010629

OTHER SOURCE(S): MARPAT 136:102190  
 GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepared Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamide in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC50 of < 50  $\mu$ M against beta-secretase.

IT **388062-20-2P 388062-33-7P 388062-99-5P**  
**388063-39-6P 388065-53-0P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

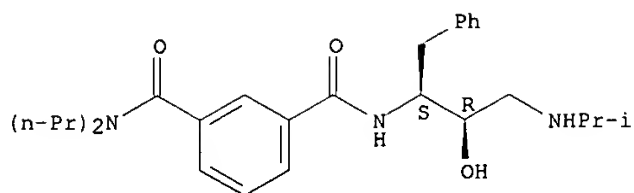
(preparation of substituted amines for treating Alzheimer's disease)

RN 388062-20-2 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(1-methylethyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

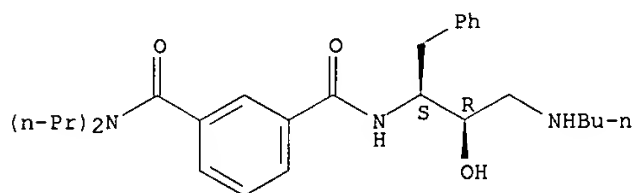
09/288,556



RN 388062-33-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

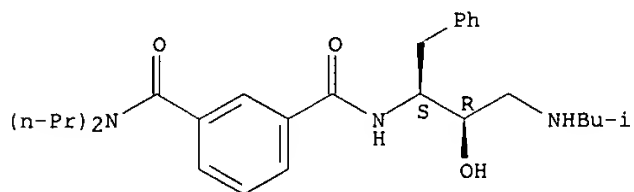
Absolute stereochemistry.



RN 388062-99-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(2-methylpropyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

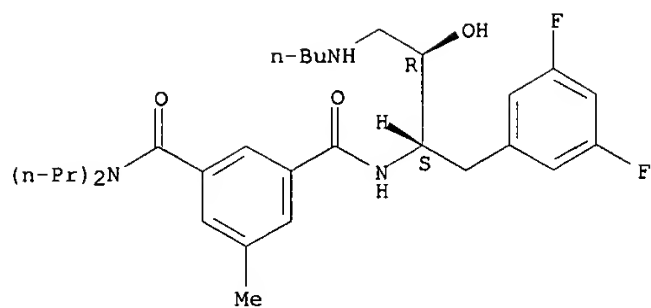


RN 388063-39-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

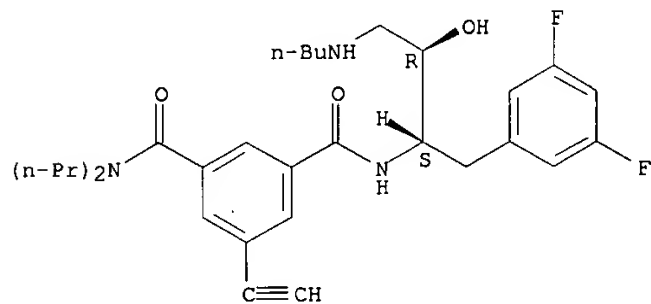
09/288,556



RN 388065-53-0 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(butylamino)-1-[(3,5-difluorophenyl)methyl]-2-hydroxypropyl]-5-ethynyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d 16 1-13 ibib abs hitstr

L6 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:143093 CAPLUS

DOCUMENT NUMBER: 140:181220

TITLE: Preparation of benzamide derivatives as  
β-secretase inhibitorsINVENTOR(S): Uchikawa, Osamu; Aso, Kazuyoshi; Koike, Tatsuki;  
Tarui, Naoki; Hirai, Keisuke

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

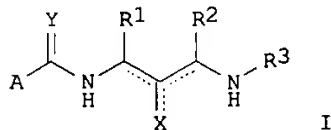
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

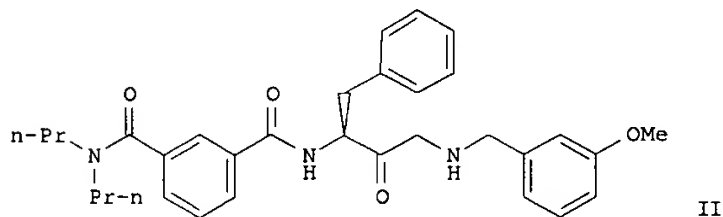
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014843	A1	20040219	WO 2003-JP10045	20030807
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: JP 2002-233231 A 20020809

GI



I



II

AB The title compds. I [wherein A = (un)substituted aryl; R1 = (un)substituted aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkyl, cycloalkyl, or cycloalkylalkyl; R2 = H, (un)substituted aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkyl, or cycloalkyl; R3 = (un)substituted arylalkyl, heteroarylalkyl, or alkyl; X = O, S, or (un)substituted NH; Y = O or S; with exclusions] or prodrugs or salts thereof are prepared as β-secretase inhibitors. For example, the compound II•HCl was

prepared in a multi-step synthesis. II•HCl showed inhibitory activity with IC<sub>50</sub> of 0.099  $\mu$ M against human  $\beta$ -secretase. I are useful for the treatment of neurodegenerative disease, neuropathy, memory disorder, psychiatric disorder, etc. (no data). Formulations containing I as an active ingredient were also described.

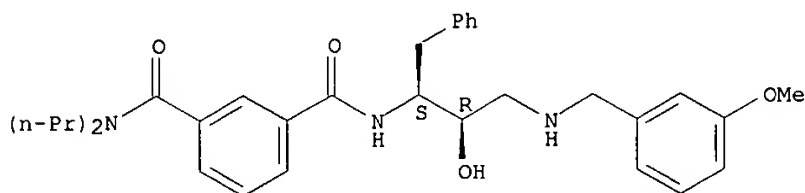
IT **388062-23-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(intermediate; preparation of benzamide derivs. as  $\beta$ -secretase inhibitors)

RN 388062-23-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[[(1S,2R)-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:2867 CAPLUS

DOCUMENT NUMBER: 140:59634

TITLE: Process for preparing 5-(1,3-oxazol-2-yl)benzoic acid derivatives

INVENTOR(S): Reeder, Michael R.; Imbordino, Rick J.

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000821	A1	20031231	WO 2003-US19585	20030620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2002-390285P P 20020620  
US 2003-450478P P 20030227



OTHER SOURCE(S): CASREACT 140:59634; MARPAT 140:59634  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Disclosed are compds. of formula (I) [R1 = C1-6 alkoxy, OH; R2, R3 = H, Ph, C1-4 alkyl; or R2 and R3 and the carbons to which they are attached form a benzo ring, which is optionally substituted with C1-4 alkyl, C1-4 alkoxy, or dialkylamino; R6 = C1-6 alkoxy or NR4R5; R4, R5 = C1-6 alkyl] and a process to prepare the compound I, by coupling a zinc chloride/optionally substituted oxazole adduct (II) (R2, R3 = same as above) and an compound of formula (III) (X = Br, iodo, OSO2CF3, OSO2Me) in the presence of a transition metal catalyst. The compds. I are used to prepare compds. of formula (IV) [R2, R3, R6 = same as above; R10 = R10 = -(CH2)1-2-S(O)0-2-(C1-6 alkyl), or each (un)substituted C1-10 alkyl, C2-6 alkenyl, or C2-6 alkynyl, aryl, heteroaryl, heterocyclyl, C1-6-alkylaryl, C1-6 alkylheteroaryl, or C1-6 alkylheterocyclyl, where the ring portions of each are optionally substituted; R20, R30 = H, each (un)substituted C1-6 alkyl, CONH2, or SO2NH2, (CH2)0-4-aryl, (CH2)0-4-heteroaryl, C2-6 alkenyl, C2-6 alkynyl, CO2H, CO2-(C1-4 alkyl); or R20, R30 and the carbon to which they are attached form a C3-7 carbocycle, wherein one carbon atom is optionally replaced by a group selected from O, S, SO2, or (un)substituted NH; Rc = H, (CR245R250)0-4-aryl, (CR245R250)0-4-heteroaryl, (CR245R250)0-4-heterocyclyl, (CR245R250)0-4-arylheteroaryl, (CR245R250)0-4-arylheterocyclyl, (CR245R250)0-4-arylaryl, (CR245R250)0-4-heteroarylaryl, (CR245R250)0-4-heteroarylheterocyclyl, (CR245R250)0-4-heteroarylheteroaryl, etc.; R245, R250 = H, C1-4 alkyl, C1-4 alkylaryl, C1-4 alkylheteroaryl, C1-4 hydroxyalkyl, C1-4 alkoxy, C1-4 haloalkoxy, (CH2)0-4-C3-7 cycloalkyl, Ph, etc.; or R245 and R250 are taken together with the carbon to which they are attached to form a C3-7 carbocycle, where one carbon atom is optionally replaced by a heteroatom selected from O, S, SO2, and (un)substituted NH] in the treatment of Alzheimer's disease and related conditions. Thus, BuLi (1.4 equiv) was added dropwise over 30 min to a stirred, cooled (-78°) mixture of 1,3-oxazole (1.3 equiv) in THF, while maintaining the mixture at a temperature below about -55°, stirred for 30 min, treated with solid ZnCl2 (3 equiv) in 3-10 portions over about 10-15 min, allowed to warm to 20-25°, and stirred for an addnl. 10 min to give a solution of 2-oxazolylzinc chloride. The latter zinc chloride adduct was added over a period of 2 h to a mixture of Me 3-bromo-5-[(dipropylamino)carbonyl]benzoate (V) and tetrakis(triphenylphosphine) palladium (5 mol%) in THF at 50°, and stirred at 50° until no V was observed by HPLC (usually about 1 h) to give, after workup and silica gel chromatog., Me 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoate (VI). VI was saponified by NaOH in aqueous MeOH and acidified with concentrated HCl to give 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoic acid which was treated with CDI in THF at room temperature for 1 h, added slowly over to a cooled (-35°) mixture of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol in THF, warmed to 0°, and stirred until the completion of the reaction was observed by HPLC to give, after workup and silica gel chromatog., N1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-[[1-(3-ethynylphenyl)cyclopropyl]amino]-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N3,N3-dipropylisophthalamide (VII).

IT 527716-71-8P

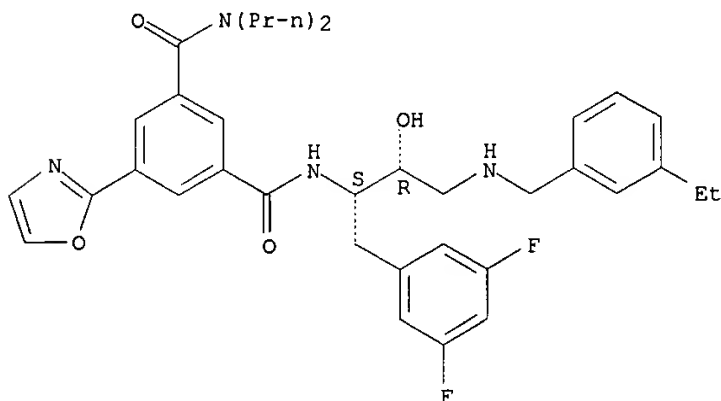
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparing oxazolylbenzoic acid derivs. as intermediates for anti-Alzheimer's agent)

RN 527716-71-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[3-(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-(2-oxazolyl)-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:696859 CAPLUS

DOCUMENT NUMBER: 139:230480

TITLE: Preparation of substituted amines prodrugs useful in treating Alzheimer's disease

INVENTOR(S): Varghese, John; Jagodzinska, Barbara; Maillard, Michel; Beck, James P.; Tenbrink, Ruth E.; Getman, Daniel

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn

SOURCE: PCT Int. Appl., 483 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072535	A2	20030904	WO 2003-US7287	20030227
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

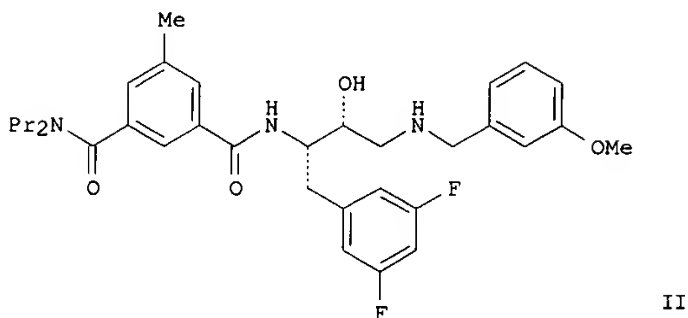
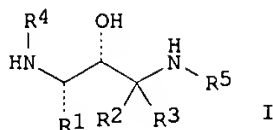
PRIORITY APPLN. INFO.:

US 2002-359953P P 20020227

OTHER SOURCE(S):

MARPAT 139:230480

GI



AB Amines [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO<sub>2</sub>, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH<sub>2</sub>)<sub>0-3</sub>cycloalkyl, etc.; e.g. N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N<sub>3</sub>,N<sub>3</sub>-dipropylisophthalamide], useful in treating Alzheimer's disease and other similar diseases, were prepared. Although the methods of preparation are not claimed, hundreds of example preps. are included. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamic acid in the presence of Et<sub>3</sub>N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II (N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N<sub>3</sub>,N<sub>3</sub>-dipropylisophthalamide). The compds. I exhibit an IC<sub>50</sub> of < 50 μM against β-secretase.

IT **388066-36-2P**, N-[(1R,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-bromo-5-methylbenzamide **388071-98-5P**, N-[(1S,2R)-1-[4-(Benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N'-[4-(benzyloxy)butyl]-5-methyl-N'-propylisophthalamide

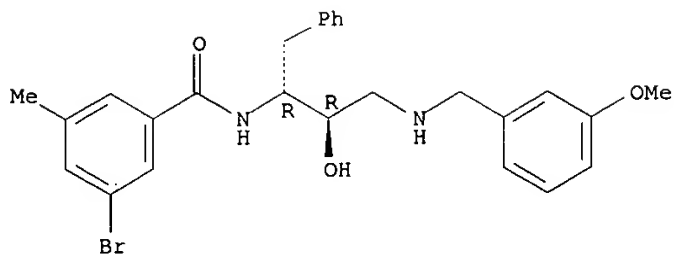
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RN 388066-36-2 CAPLUS

CN Benzamide, 3-bromo-N-[(1R,2R)-2-hydroxy-3-[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

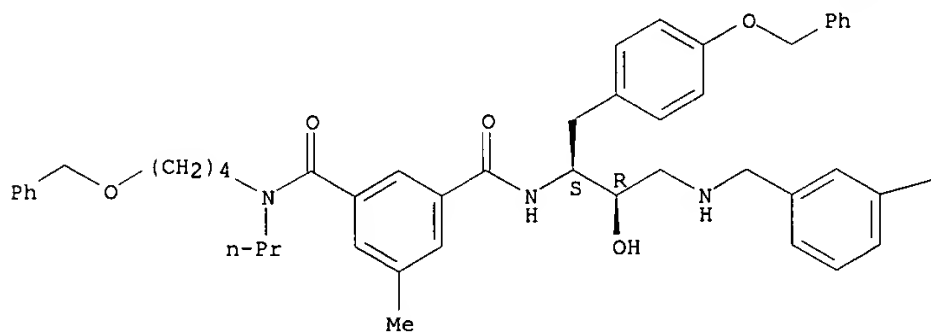


RN 388071-98-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl)methyl]amino]-1-[[4-(phenylmethoxy)phenyl)methyl]propyl]-5-methyl-N-[4-(phenylmethoxy)butyl]-N-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

— OMe

IT **388062-16-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide  
**388062-17-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(2-furyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide  
**388062-19-9P**, N-[(1S,2R)-1-Benzyl-3-(benzylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-21-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-(4-toluidino)propyl]-N',N'-dipropylisophthalamide  
**388062-22-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(4-methoxyphenyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide  
**388062-23-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide  
**388062-26-8P**, N-[(1S,2R)-1-Benzyl-3-[(2-chlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-27-9P**,

N-[(1S,2R)-1-Benzyl-3-[(4-chlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-29-1P**, N-[(1S,2R)-1-Benzyl-3-(2,3-dihydro-1H-inden-1-ylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-31-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(tetrahydro-2-furanylmethyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-34-8P**, N-[(1S,2R)-1-Benzyl-3-(cyclohexylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-35-9P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(2-pyridinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-36-0P**, N-[(1S,2R)-3-[(2-Aminobenzyl)amino]-1-benzyl-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-37-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-pyridinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-38-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(1-pyrrolidinyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-43-9P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-phenylpropyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-48-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(4-phenylbutyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-49-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-51-9P**, N-[(1S,2R)-1-Benzyl-3-[(3-chlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-52-0P**, N-[(1S,2R)-1-Benzyl-3-[[2-(4-chlorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-53-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(2-pyridinyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-54-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-(pyridinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-56-4P**, N-[(1S,2R)-1-Benzyl-3-[(2,3-dimethylbenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-57-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(trifluoromethoxy)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-58-6P**, N-[(1S,2R)-1-Benzyl-3-[[2-(2-chloro-6-phenoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-59-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-(trifluoromethyl)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-60-0P**, N-[(1S,2R)-1-Benzyl-3-[(2,3-dichlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-61-1P**, N-[(1S,2R)-1-Benzyl-3-[(3,5-dichlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-62-2P**, N-[(1S,2R)-1-Benzyl-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-63-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-(trifluoromethoxy)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-64-4P**, N-[(1S,2R)-3-[[2-[4-(Aminosulfonyl)phenyl]ethyl]amino]-1-benzyl-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-65-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(4-methoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-66-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(4-methylbenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-67-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3,4,5-trimethoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-68-8P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-(trifluoromethoxy)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-69-9P**, N-[(1S,2R)-1-Benzyl-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-70-2P**, N-[(1S,2R)-1-Benzyl-3-[(2,4-dimethoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-71-3P**, N-[(1S,2R)-1-Benzyl-3-[[[(1,1'-biphenyl)-3-yl]methyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-72-4P**, N-[(1S,2R)-1-Benzyl-3-[(3,4-dichlorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-73-5P**, N-[(1S,2R)-1-Benzyl-3-[(2-fluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-74-6P**,

N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-(trifluoromethyl)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-75-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(methylbenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388062-78-0P**, N-[(1S,2R)-1-Benzyl-3-[[3,5-bis(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-79-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(trifluoromethyl)benzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-82-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[4-hydroxy-3-methoxybenzyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-83-7P**, N-[(1S,2R)-1-Benzyl-3-[[3,4-dihydroxybenzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-88-2P**, N-[(1S,2R)-1-Benzyl-3-[[2-(2-fluorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-89-3P**, N-[(1S,2R)-1-Benzyl-3-[[2-(3-fluorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-90-6P**, N-[(1S,2R)-1-Benzyl-3-[[2-(4-fluorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-91-7P**, N-[(1S,2R)-1-Benzyl-3-[[2-(4-bromophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-92-8P**, N-[(1S)-1-Benzyl-2-hydroxy-3-[[2-(3-methoxyphenyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-93-9P**, N-[(1S,2R)-1-Benzyl-3-[[2-(2,4-dichlorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-94-0P**, N-[(1S,2R)-1-Benzyl-3-[[2-(3-chlorophenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-95-1P**, N-[(1S)-1-Benzyl-3-[[2-(2,5-dimethoxyphenyl)ethyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388062-96-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(4-methylphenyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388062-98-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[3-(4-morpholinyl)propyl]amino]propyl]-N',N'-dipropylisophthalamide **388063-00-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(4-morpholinyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388063-02-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[2-(2-thienyl)ethyl]amino]propyl]-N',N'-dipropylisophthalamide **388063-05-6P**, N-[(1S,2R)-1-Benzyl-3-[[2,4-dichlorobenzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-07-8P**, N-[(1S,2R)-1-Benzyl-3-[[4-tert-butylbenzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-09-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[1-(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino]propyl]-N',N'-dipropylisophthalamide **388063-10-3P**, N-[(1S,2R)-1-Benzyl-3-[[3,4-dimethylbenzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-18-1P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-22-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[4-(dimethylamino)benzyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-26-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[3-(pyridinyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-32-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[2-phenylethyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-38-5P**, N-[(1S,2R)-3-(Cyclohexylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-43-2P**, N-[(1S,2R)-3-[[3-Chlorobenzyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-44-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[3-methoxybenzyl]amino]propyl]-3-[[2-propylpentyl]sulfonyl]benzamide **388063-45-4P**, N-[(1S,2R)-3-[[[1,1'-Biphenyl]-3-yl]methyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-46-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[3-iodobenzyl]amino]propyl]-5-methyl-N',N'-

dipropylisophthalamide **388063-47-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-49-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1,3-thiazol-5-yl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-50-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-thienyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-51-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-52-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-pyrazinyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-53-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-54-5P**, N-[(1S,2R)-3-[(1,3-Benzodioxol-5-yl)methyl]amino]-1-benzyl-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-55-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-56-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-(trifluoromethyl)benzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-57-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-58-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-(trifluoromethoxy)benzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-59-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-fluorobenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-60-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-61-4P**, N-[(1S,2R)-3-[(3-Bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-62-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(5-methyl-2-furyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-64-7P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methoxy-N',N'-dipropylisophthalamide **388063-65-8P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-66-9P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-chloro-N',N'-dipropylisophthalamide **388063-68-1P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-fluoro-N',N'-dipropylisophthalamide **388063-72-7P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-[(4-morpholinyl)carbonyl]benzamide **388063-73-8P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methylbenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388063-80-7P**, 3-Benzoyl-N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]benzamide **388063-81-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl][1,1'-biphenyl]-3-carboxamide **388063-82-9P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N'-(2-methoxyethyl)-N'-propylisophthalamide **388063-83-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-ethoxybenzamide **388063-84-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-2-naphthamide **388063-85-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1R)-1,2,3,4-tetrahydronaphthalen-1-yl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388063-86-3P**, N-[(1R)-3-[(3,5-Bis(trifluoromethyl)benzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388063-87-4P**,

N-[(1S,2R)-1-Benzyl-3-[[2-fluoro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-88-5P**,  
 N-[(1S,2R)-1-Benzyl-3-[(2,3-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-89-6P**, N-[(1S,2R)-1-Benzyl-3-[[3-fluoro-4-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-90-9P**, N-[(1S,2R)-1-Benzyl-3-[(2,5-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-91-0P**, N-[(1S,2R)-1-Benzyl-3-[[3-fluoro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-92-1P**, N-[(1S,2R)-1-Benzyl-3-[(3,4-difluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-93-2P**, N-[(1S,2R)-1-Benzyl-3-[[4-fluoro-3-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-94-3P**, N-[(1S,2R)-1-Benzyl-3-[[2-chloro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-95-4P**, N-[(1S,2R)-1-Benzyl-3-[[4-chloro-3-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-96-5P**, N-[(1S,2R)-1-Benzyl-3-(2,3-dihydro-1H-inden-2-ylamino)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-97-6P**, N-[(1S)-1-Benzyl-2-hydroxy-3-[(3-nitrobenzyl)amino]propyl]-N',N'-dipropylisophthalamide **388063-98-7P**, N-[(1S,2R)-1-Benzyl-3-[[3-(difluoromethoxy)benzyl]amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388063-99-8P**, N-[(1S,2R)-1-Benzyl-3-[(3-ethoxybenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388064-00-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[[5-methyl-2-pyrazinyl)methyl]amino]propyl]-N',N'-dipropylisophthalamide **388064-01-5P**, N-[(1S,2R)-1-Benzyl-3-[(3-bromo-4-fluorobenzyl)amino]-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388064-02-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,5-dimethylbenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-03-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethoxybenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-05-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isobutoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-06-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[4-methyl-1,3-thiazol-2-yl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-07-1P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N'-methyl-N'-propylisophthalamide **388064-13-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1R)-7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-14-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1S)-7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-15-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-(dimethylamino)benzamide **388064-16-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-2-methyl-1H-benzimidazole-5-carboxamide **388064-17-3P**, 3-(Aminosulfonyl)-N-[(1S)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-chlorobenzamide **388064-18-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-cyanobenzamide **388064-19-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-chloro-3-nitrobenzamide **388064-20-8P**, Methyl 3-[[[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino]carbonyl]-5-nitrobenzoate **388064-21-9P**, tert-Butyl [3-[[[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino]carbonyl]phenyl]carbamate **388064-22-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-9,10-dioxo-9,10-dihydro-2-



anthracenecarboxamide **388064-23-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1H-1,2,3-benzotriazole-6-carboxamide **388064-24-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide **388064-25-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1H-indole-5-carboxamide **388064-26-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-fluoro-5-(trifluoromethyl)benzamide **388064-27-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-(trifluoromethyl)benzamide **388064-28-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-(butylamino)benzamide **388064-29-7P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-(trifluoromethoxy)benzamide **388064-30-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-dimethoxybenzamide **388064-31-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-dimethylbenzamide **388064-32-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-difluorobenzamide **388064-33-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3,5-dichlorobenzamide **388064-34-4P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-(benzyloxy)benzamide **388064-35-5P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1,3-benzodioxole-5-carboxamide **388064-36-6P**, 3-(Acetylamino)-N-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]benzamide **388064-37-7P**, 4-(Acetylamino)-N-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]benzamide **388064-38-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[3,5-dimethyl-4-isoxazolyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-39-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-phenylpropyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-40-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[3-furyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-42-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-propoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-43-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-pyridinyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-44-6P**, N-[(1S,2R)-3-(Benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-hydroxy-N',N'-dipropylisophthalamide **388064-46-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1S)-1,2,3,4-tetrahydronaphthalen-1-yl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-47-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(2,5-dimethylbenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-48-0P**, N-[(1S,2R)-3-[[2-Chloro-5-(trifluoromethyl)benzyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-49-1P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-5-methylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-50-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-51-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(1R)-2,3-dihydro-1H-inden-1-ylamino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-53-7P**, N-[(1S,2R)-3-[[1-Benzofuran-2-yl)methyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-55-9P**, N-[(1S,2R)-1-(4-Fluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388064-56-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[butyl(butyryl)amino]-5-methylbenzamide **388064-57-1P**, N-[1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-methyl-N',N'-

dipropylisophthalamide **388064-58-2P**, N'-[1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-methyl-N,N-dipropylisophthalamide  
**388064-59-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-4-methyl-N',N'-dipropylisophthalamide  
**388064-60-6P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1-butyl-1H-indole-6-carboxamide  
**388064-61-7P**, N-[(1S,2R)-3-Anilino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388064-62-8P**  
, 5-Bromo-N-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N',N'-dipropylisophthalamide **388064-65-1P**,  
N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-hydroxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide  
**388064-66-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-cyano-N',N'-dipropylisophthalamide  
hydrochloride **388064-67-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropyl-1,3,5-benzenetricarboxamide  
**388064-70-8P**, 5-(Aminosulfonyl)-N-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropylisophthalamide  
**388064-71-9P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropyl-5-[(1-pyrrolidinyl)sulfonyl]isophthalamide **388064-72-0P**,  
N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-[(methylamino)sulfonyl]-N',N'-dipropylisophthalamide **388064-73-1P**  
, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-[(dimethylamino)sulfonyl]-N',N'-dipropylisophthalamide  
**388064-96-8P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-ethyl-N',N'-dipropylisophthalamide  
**388064-97-9P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-isobutyl-N',N'-dipropylisophthalamide  
**388064-98-0P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-tert-butyl-N',N'-dipropylisophthalamide  
**388064-99-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-cyano-N'-propylisophthalamide  
**388065-00-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dipropyl-1,3,5-benzenetricarboxamide  
**388065-01-8P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N',N'-dimethyl-N',N'-dipropyl-1,3,5-benzenetricarboxamide **388065-04-1P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N'-propyl-1,3,5-benzenetricarboxamide **388065-05-2P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(butyryl)(propyl)amino]-5-methylbenzamide **388065-06-3P**, N-[(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1-propyl-1H-indole-6-carboxamide  
**388065-07-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1-propyl-1H-indole-6-carboxamide  
**388065-08-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3,4-dimethylbenzyl)amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-09-6P**, N-[(1S,2R)-3-[(3-Aminobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-13-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide  
**388065-14-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-3-methylbenzamide **388065-15-4P**,  
N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1H-isoindol-3-yl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide  
**388065-16-5P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-19-8P**,  
N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-

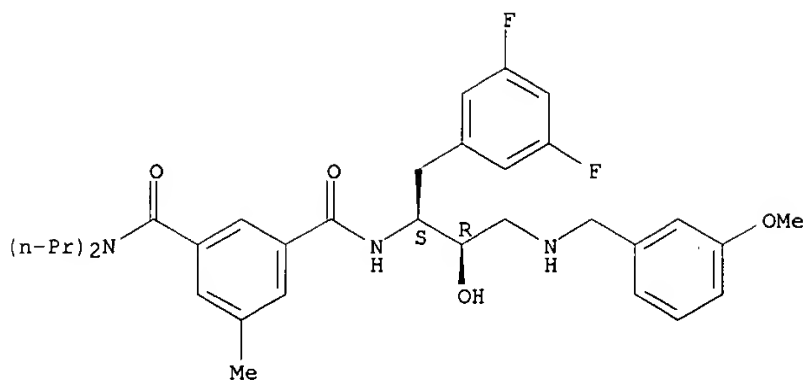
hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-20-1P**  
 , N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[3-(dimethylamino)benzyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-21-2P**  
 , N-[(1S,2R)-1-(3,5-Difluorobenzyl)-3-[[4,5-dimethyl-2-furyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-22-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopentyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-23-4P**, N-[(1S,2R)-3-(Cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-24-5P**, N-[(1S,2R)-3-[(Cyclopropylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N',N'-dipropylisophthalamide **388065-27-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(tetrahydro-3-furanylmethyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-29-0P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-oxo-3-azepanyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-30-3P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[3-methyl-2-furyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-31-4P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[[[(2S)-tetrahydrofuran-2-yl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-33-6P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropenylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-36-9P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide **388065-37-0P**, Methyl 4-[[[(2R,3S)-4-(3,5-difluorophenyl)-3-[[3-[(dipropylamino)carbonyl]-5-methylbenzoyl]amino]-2-hydroxybutyl]amino]methyl]benzoate **388065-39-2P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(5-isoxazolyl)methyl]amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-42-7P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(2-methoxybenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-43-8P**, N-[(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl]-5-methyl-N',N'-dipropylisophthalamide **388065-44-9P**, 4-(Butyrylamino)-N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]benzamide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of substituted amine prodrugs useful in treating Alzheimer's disease)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-(9CI) (CA INDEX NAME)

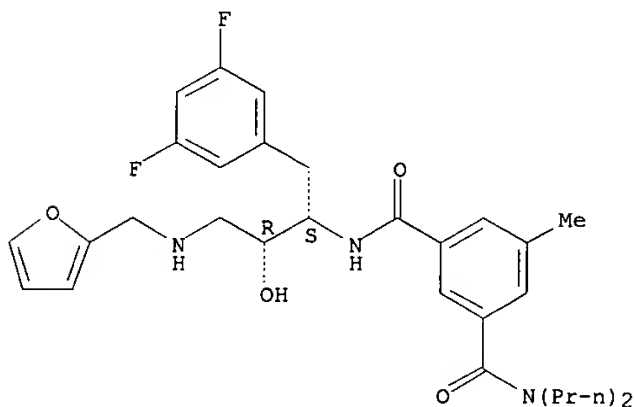
Absolute stereochemistry.



RN 388062-17-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(2-furanylmethyl)amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

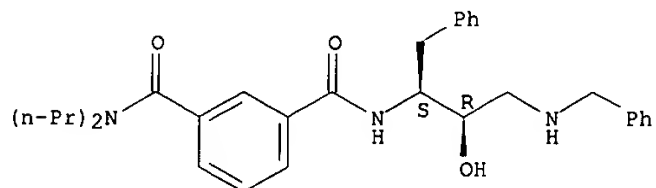
Absolute stereochemistry.



RN 388062-19-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



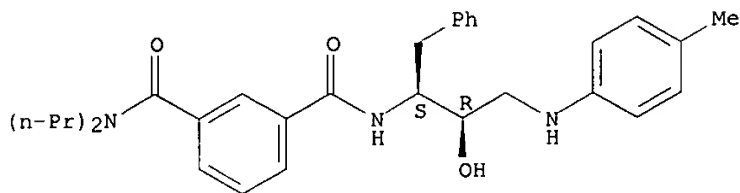
RN 388062-21-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(4-methylphenyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

09/288,556

1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

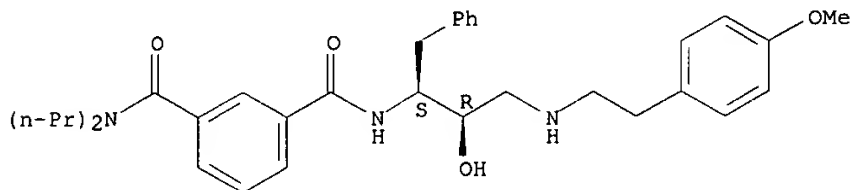
Absolute stereochemistry.



RN 388062-22-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[2-(4-methoxyphenyl)ethyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

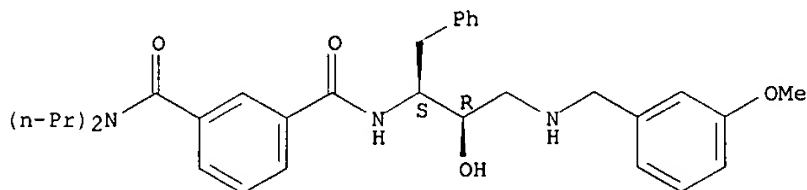
Absolute stereochemistry.



RN 388062-23-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

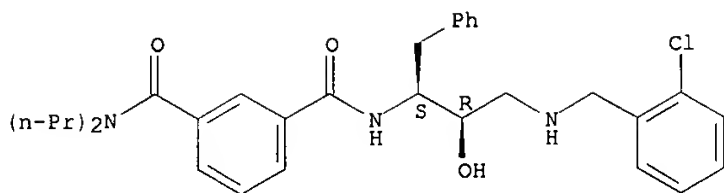
Absolute stereochemistry.



RN 388062-26-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[2-(2-chlorophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

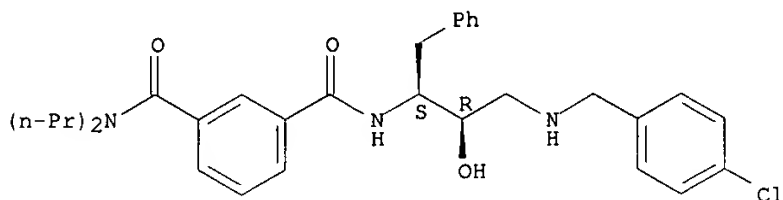
Absolute stereochemistry.



RN 388062-27-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'--[(1S,2R)-3-[[4-chlorophenyl)methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

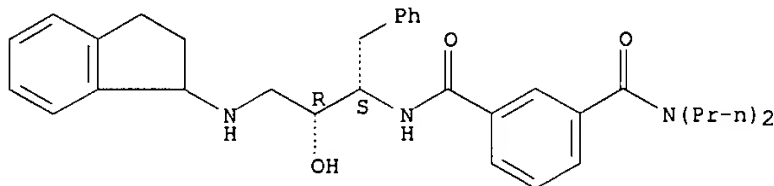
Absolute stereochemistry.



RN 388062-29-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'--[(1S,2R)-3-[(2,3-dihydro-1H-inden-1-yl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

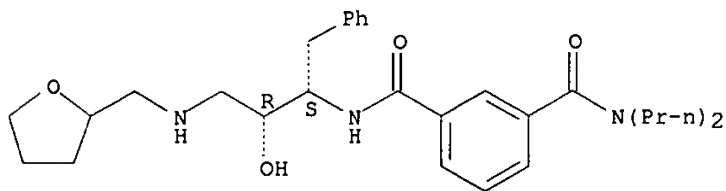
Absolute stereochemistry.



RN 388062-31-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'--[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[tetrahydro-2-furanyl)methyl]amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

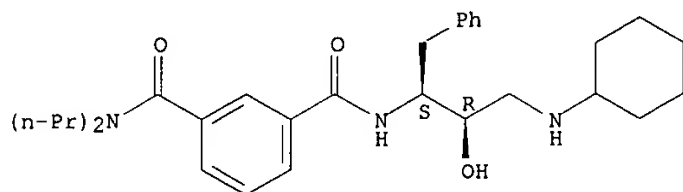


RN 388062-34-8 CAPLUS

09/288,556

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(cyclohexylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:472477 CAPLUS

DOCUMENT NUMBER: 139:52753

TITLE: Preparation of substituted hydroxyethylamines as  $\beta$ -secretase inhibitors

INVENTOR(S): Tenbrink, Ruth; Maillard, Michel; Warpehoski, Martha

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia &amp; Upjohn Company

SOURCE: PCT Int. Appl., 306 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

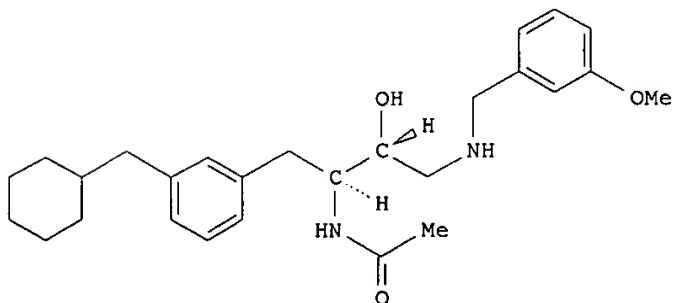
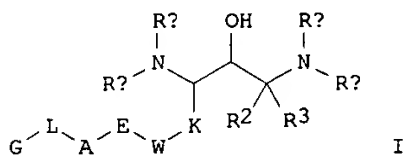
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050073	A1	20030619	WO 2002-US39050	20021206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004044072	A1	20040304	US 2002-313849	20021206
PRIORITY APPLN. INFO.:		US 2001-338452P	P	20011206
OTHER SOURCE(S):		MARPAT 139:52753		

GI





AB Title compds. I [E = bond, alkylene; RA = H, benzyloxycarbonyl; RD = H, alkoxycarbonyl; K = (un)substituted alkyl; A = aryl, cycloalkyl, heteroaryl, etc.; W = bond, SOO-2, (un)substituted amino; L = bond, absent, etc.; G = absent, alkyl, cycloalkyl, etc.; R2-3 = H, alkyl, aryl, etc.; RN = Ph naphthyl, tetralinyl, etc.; RC = heteroaryl, etc.] are prepared as  $\beta$ -secretase inhibitors. For instance, N-[(1S,2R)-1-[3-(cyclohexylmethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]acetamide (II) isolated as the HCl salt is prepared in several steps. The key intermediate in the synthesis is derived from the asym. hydrogenation of Me 2-[[ (benzyloxy)carbonyl]amino]-3-(2-bromophenyl)acrylate (preparation given) to give the corresponding phenylalanine analog intermediate. I are useful for the treatment of Alzheimer's disease.

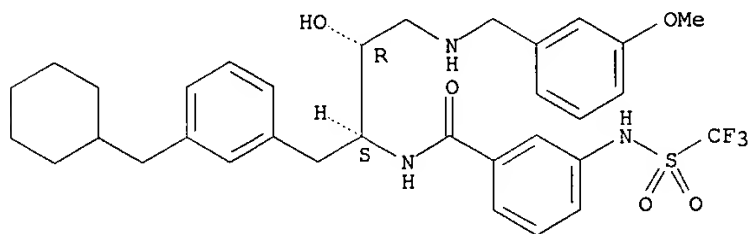
IT 527722-73-2P 527722-74-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of substituted hydroxyethylamines as  $\beta$ -secretase inhibitors)

RN 527722-73-2 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[[3-methoxyphenyl]methyl]amino]propyl]-3-[[ (trifluoromethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

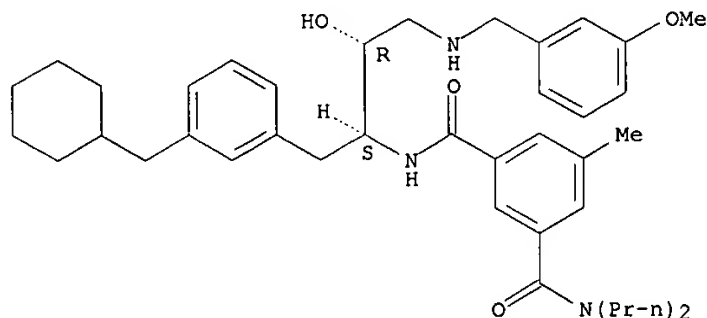
Absolute stereochemistry.



RN 527722-74-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[[3-methoxyphenyl]methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 527730-33-2P 546115-11-1P 546115-12-2P

**546115-31-5P 546115-32-6P**

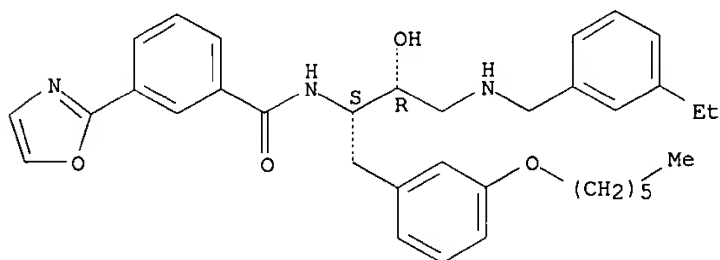
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted hydroxyethylamines as  $\beta$ -secretase inhibitors)

RN 527730-33-2 CAPLUS

CN Benzamide, N-[(1S,2R)-3-[[[(3-ethylphenyl)methyl]amino]-1-[[3-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-3-(2-oxazolyl)- (9CI) (CA INDEX NAME)

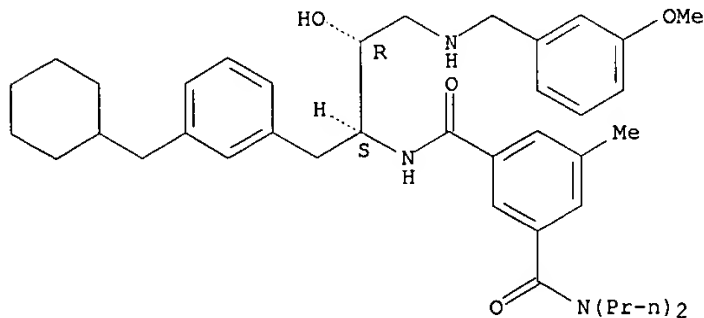
Absolute stereochemistry.



RN 546115-11-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[[[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



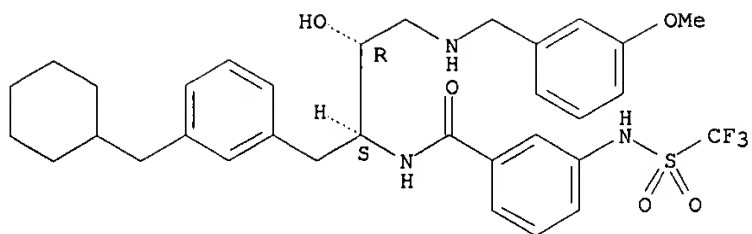
● HCl

RN 546115-12-2 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[[3-(cyclohexylmethyl)phenyl]methyl]-2-hydroxy-3-[[[(3-methoxyphenyl)methyl]amino]propyl]-3-[[[(trifluoromethyl)sulfonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/288,556

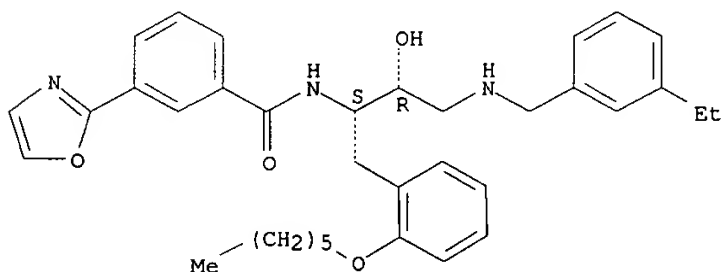


● HCl

RN 546115-31-5 CAPLUS

CN Benzamide, N-[(1S,2R)-3-[[[(3-ethylphenyl)methyl]amino]-1-[[2-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-3-(2-oxazolyl)- (9CI) (CA INDEX NAME)

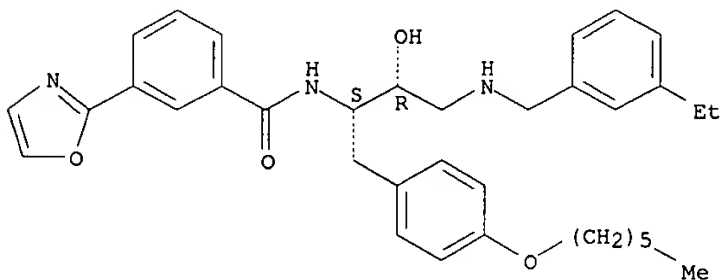
Absolute stereochemistry.



RN 546115-32-6 CAPLUS

CN Benzamide, N-[(1S,2R)-3-[[[(3-ethylphenyl)methyl]amino]-1-[[4-(hexyloxy)phenyl]methyl]-2-hydroxypropyl]-3-(2-oxazolyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

12

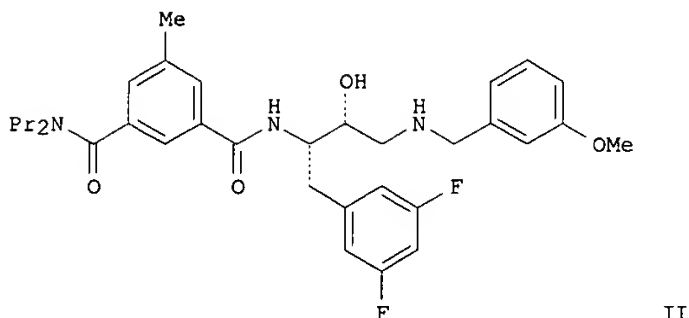
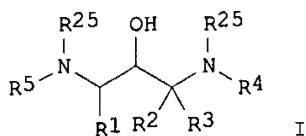
THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILAB

L6 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2003:412801 CAPLUS  
 DOCUMENT NUMBER: 139:245782  
 TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease  
 INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy  
 PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company  
 SOURCE: PCT Int. Appl., 1243 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
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WO 2003040096	A2	20030515	WO 2002-US36072	20021108
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:  
 US 2001-337122P P 20011108  
 US 2001-344086P P 20011228  
 US 2002-345635P P 20020103  
 WO 2002-US36072 A 20021108

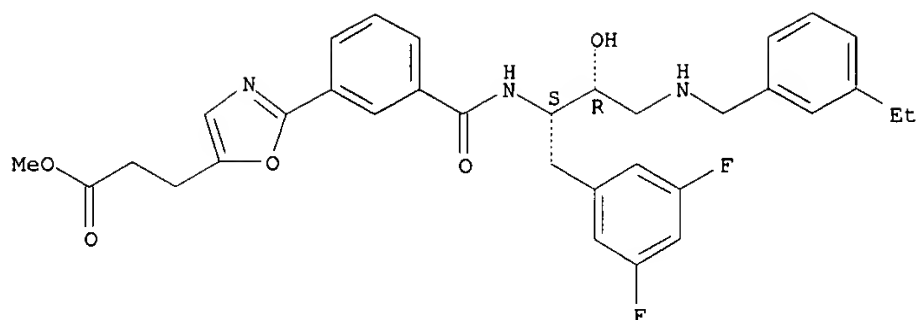
OTHER SOURCE(S): MARPAT 139:245782  
 GI



- AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO<sub>2</sub>, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO<sub>2</sub>, (un)substituted CH<sub>2</sub>; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC<sub>50</sub> of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.
- IT **527728-59-2P 527731-65-3P 527733-02-4P**  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)
- RN 527728-59-2 CAPLUS
- CN 5-Oxazolepropanoic acid, 2-[3-[[[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]amino]carbonyl]phenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

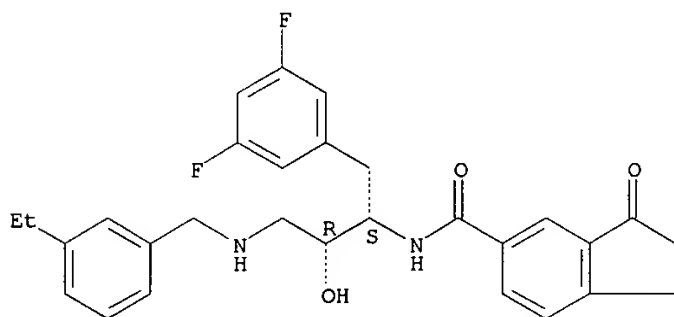
09/288,556



RN 527731-65-3 CAPLUS

CN 1H-Indene-5-carboxamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-2,3-dihydro-3-oxo- (9CI) (CA INDEX NAME)

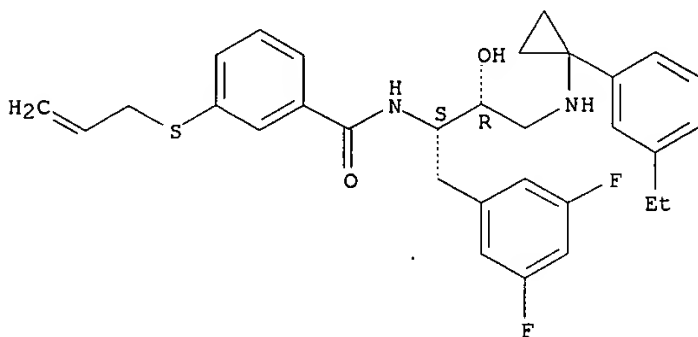
Absolute stereochemistry.



RN 527733-02-4 CAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[1-(3-ethylphenyl)cyclopropyl]amino]-2-hydroxypropyl]-3-(2-propenylthio)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 388062-16-6P 388062-17-7P 388064-67-3P  
388064-70-8P 388064-96-8P 388065-05-2P

388065-48-3P 388065-54-1P 388066-12-4P  
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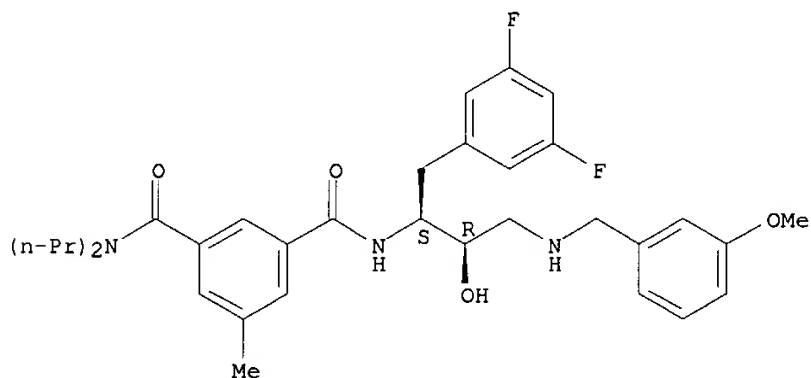
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating  
 Alzheimer's disease)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-  
 hydroxy-3-[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

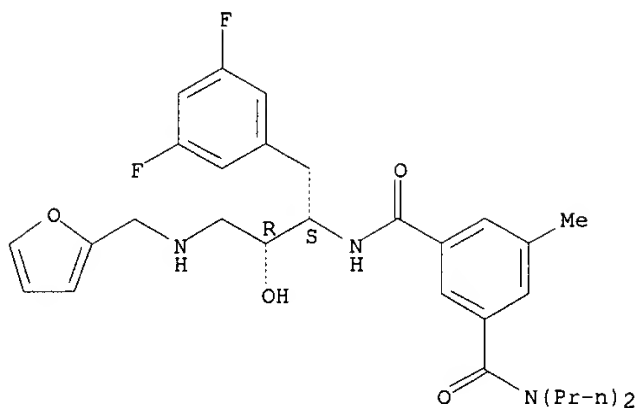


RN 388062-17-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(2-  
 furanylmethyl)amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

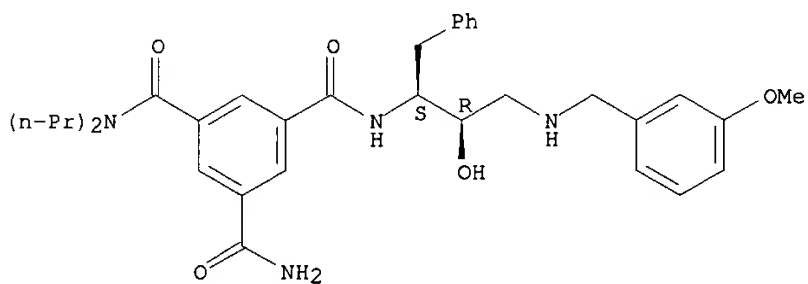




RN 388064-67-3 CAPLUS

CN 1,3,5-Benzenetricarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

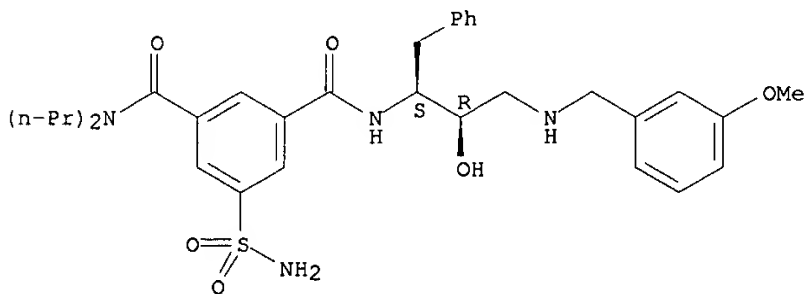
Absolute stereochemistry.



RN 388064-70-8 CAPLUS

CN 1,3-Benzenedicarboxamide, 5-(aminosulfonyl)-N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

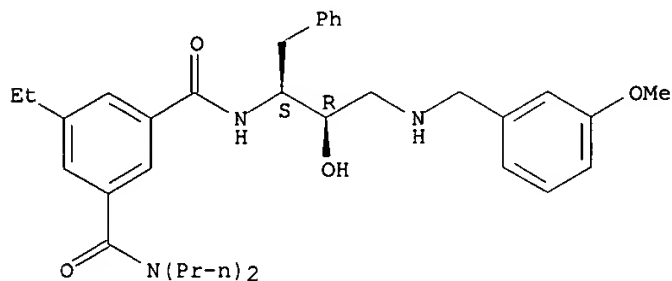


RN 388064-96-8 CAPLUS

09/288,556

CN 1,3-Benzenedicarboxamide, 5-ethyl-N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

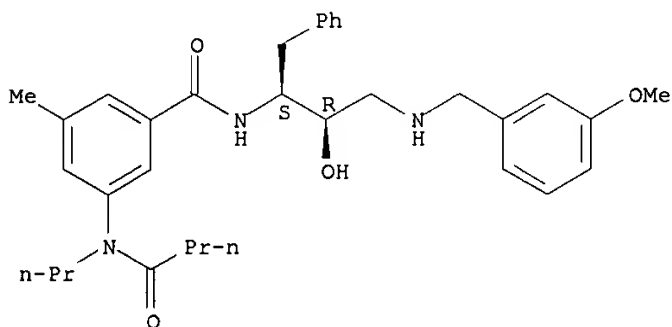
Absolute stereochemistry.



RN 388065-05-2 CAPLUS

CN Benzamide, N-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-3-methyl-5-[(1-oxobutyl)propylamino]- (9CI) (CA INDEX NAME)

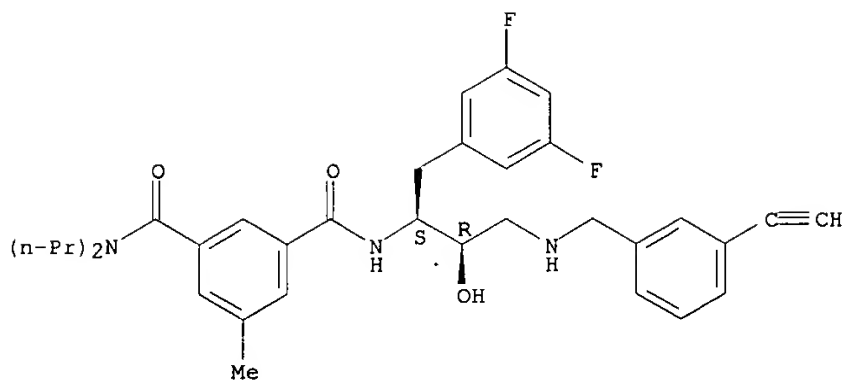
Absolute stereochemistry.



RN 388065-48-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[3-ethynylphenyl)methyl]amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

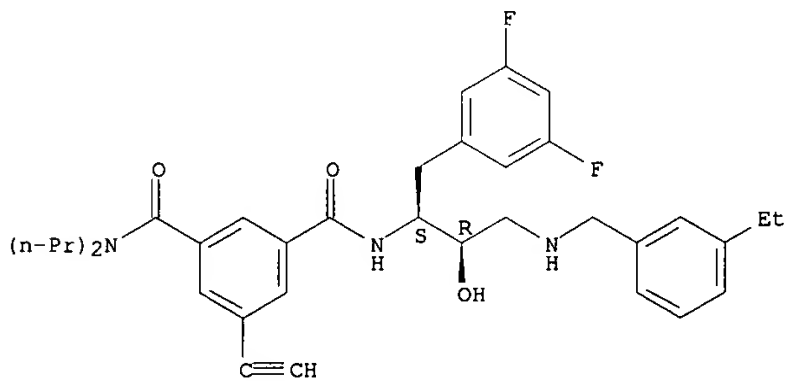
Absolute stereochemistry.



RN 388065-54-1 CAPLUS

CN 1,3-Benzenedicarboxamide, N'--[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[ (3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-ethynyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:832774 CAPLUS

DOCUMENT NUMBER: 137:325641

TITLE: Processes for the synthesis of amino acid-related  
benzyl epoxides used in the production of  
pharmaceutical agents

INVENTOR(S): Reeder, Michael R.

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn  
Company

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

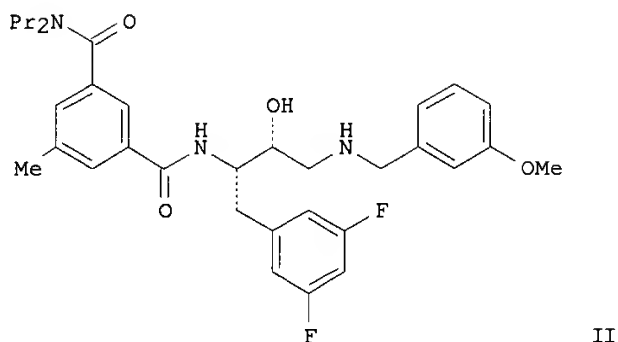
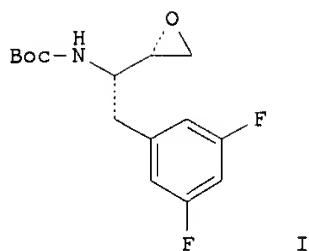
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002085877	A2	20021031	WO 2002-US12591	20020423
WO 2002085877	A3	20030306		
W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
US 2003004360	A1	20030102	US 2002-128122	20020423
EP 1381597	A2	20040121	EP 2002-728882	20020423
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
PRIORITY APPLN. INFO.:			US 2001-285772P P 20010423	
			WO 2002-US12591 W 20020423	
OTHER SOURCE(S):		CASREACT 137:325641; MARPAT 137:325641		
GI				



AB The invention provides amino acids  $R_3ONHCH(CH_2R)CO_2R_1$  [ $R$  = (un)substituted phenyl;  $R_1$  = allyl or (un)substituted alkyl, Ph, or benzyl;  $R_3O$  = H or a protecting group], amino alcs.  $H_2NCH(CH_2R)CH(OH)CH_2R_2$  [ $R_2$  = Cl, Br, trialkylsilyl, or tri-substituted aminosilyl], corresponding epoxides, and other intermediates used in the production of pharmaceutical agents. Thus, Boc-protected 3,5-difluoro-L-phenylalanine underwent sequential Me esterification, reaction with  $ClCH_2I$ , borohydride reduction, and conversion to epoxide I (KOH/EtOH). Ring opening of I with 3-methoxybenzylamine, deprotection, and acylation with 5-methyl-N,N-dipropylisophthalamide acid afforded amino alc. derivative II.

IT **388062-16-6P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

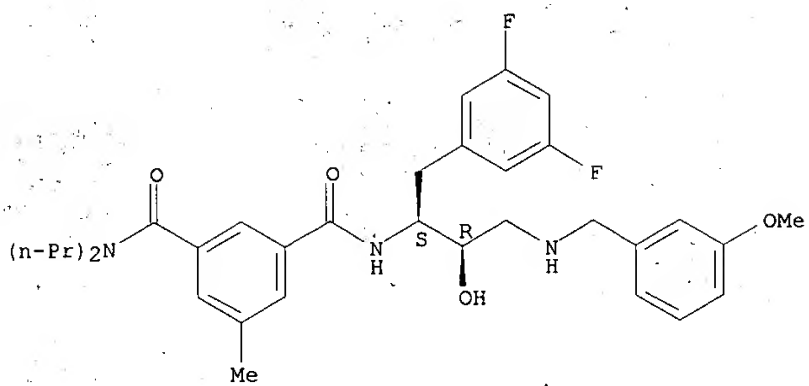
(synthesis of amino acid-related benzyl epoxides for production of pharmaceuticals)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

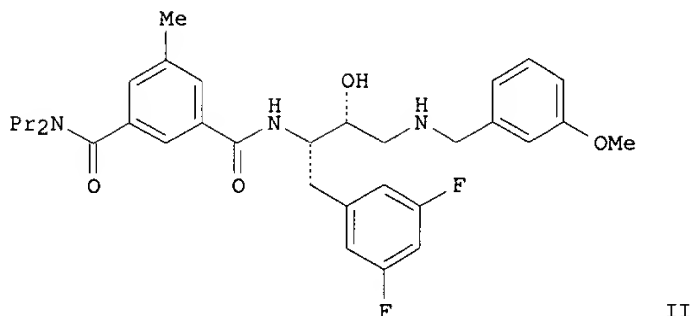
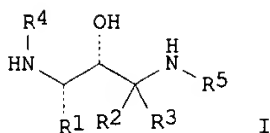
09/288,556



09/288,556

ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2002:31402 CAPLUS  
DOCUMENT NUMBER: 136:102190  
TITLE: Preparation of substituted amines to treat Alzheimer's disease  
INVENTOR(S): Maillaird, Michel; Hom, Court; Gailunas, Andrea; Jagodzinska, Barbara; Fang, Lawrence Y.; John, Varghese; Freskos, John N.; Pulley, Shon R.; Beck, James P.; Tenbrink, Ruth E.  
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company  
SOURCE: PCT Int. Appl., 651 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002512	A2	20020110	WO 2001-US21012	20010629
WO 2002002512	A3	20030821		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002128255	A1	20020912	US 2001-896139	20010629
BR 2001012000	A	20030603	BR 2001-12000	20010629
EP 1353898	A2	20031022	EP 2001-952378	20010629
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004502669	T2	20040129	JP 2002-507769	20010629
NO 2002006199	A	20030221	NO 2002-6199	20021223
PRIORITY APPLN. INFO.:			US 2000-215323P	P 20000630
			US 2000-252736P	P 20001122
			US 2000-255956P	P 20001215
			US 2001-268497P	P 20010213
			US 2001-279779P	P 20010329
			US 2001-295589P	P 20010604
			WO 2001-US21012	W 20010629
OTHER SOURCE(S):		MARPAT 136:102190		
GI				



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.], useful in treating Alzheimer's disease and other similar diseases, were prepared Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamide in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II. The compds. I exhibit an IC50 of < 50  $\mu$ M against beta-secretase.

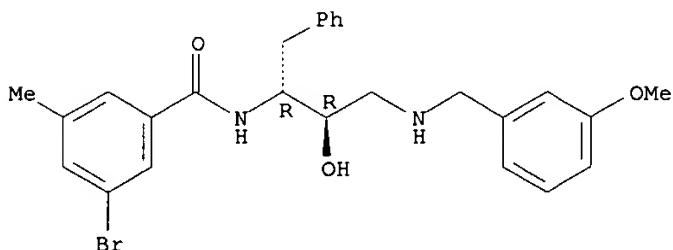
IT **388066-36-2P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of substituted amines for treating Alzheimer's disease)

RN 388066-36-2 CAPLUS

CN Benzamide, 3-bromo-N-[(1R,2R)-2-hydroxy-3-[[3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **388062-16-6P 388062-17-7P 388062-19-9P**  
**388062-21-3P 388062-22-4P 388062-23-5P**



388062-26-8P 388062-27-9P 388062-29-1P  
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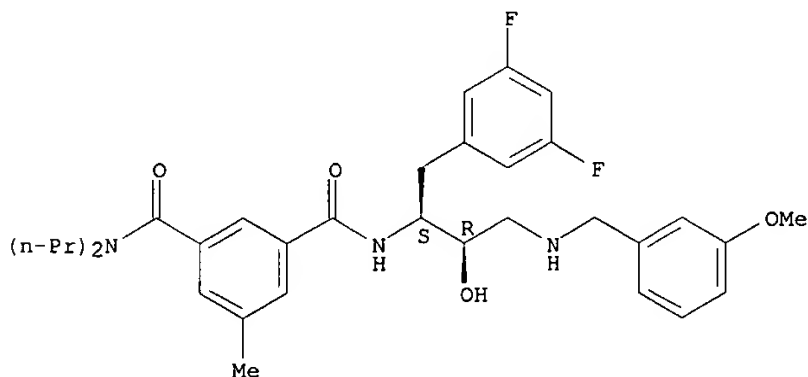
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of substituted amines for treating Alzheimer's disease)

RN 388062-16-6 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[ (3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

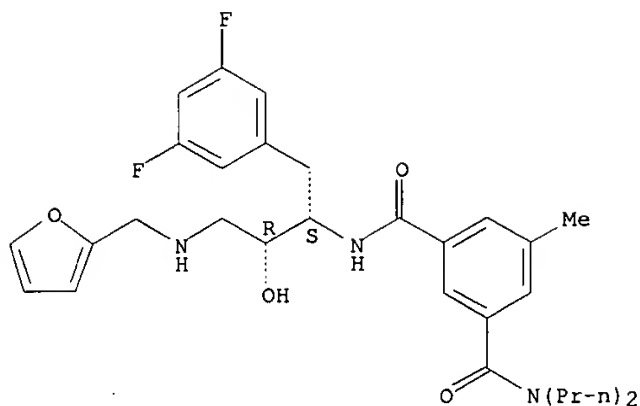
Absolute stereochemistry.



RN 388062-17-7 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[(2-furanylmethyl)amino]-2-hydroxypropyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

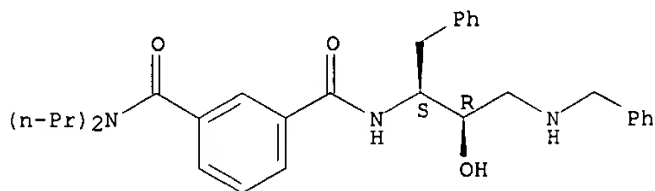
Absolute stereochemistry.



RN 388062-19-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(2,4-difluorophenyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

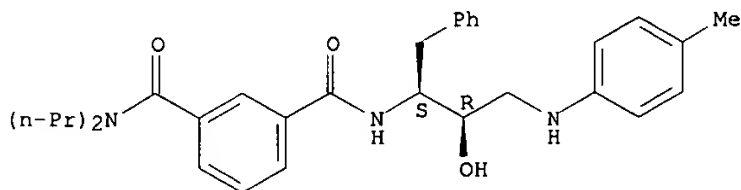
Absolute stereochemistry.



RN 388062-21-3 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[(4-methylphenyl)amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

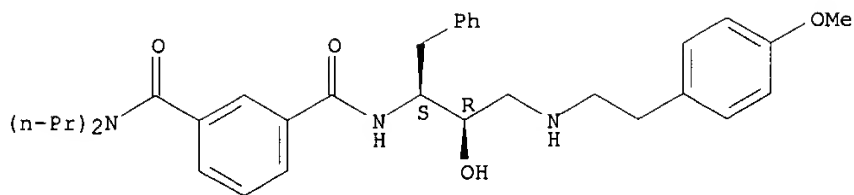


RN 388062-22-4 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[2-(4-methoxyphenyl)ethyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

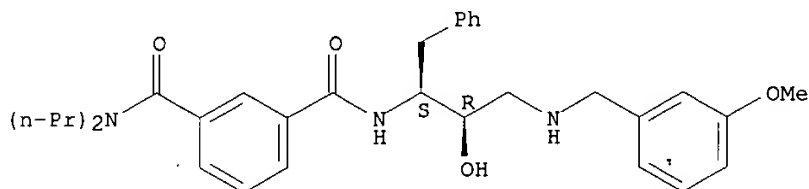
09/288,556



RN 388062-23-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-3-[[3-methoxyphenyl]methyl]amino]-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI)  
(CA INDEX NAME)

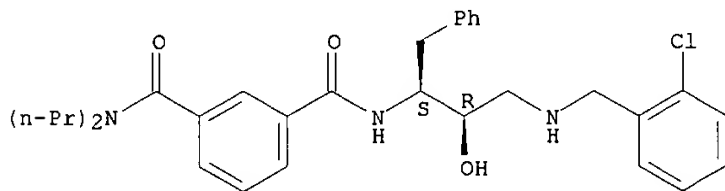
Absolute stereochemistry.



RN 388062-26-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[2-chlorophenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

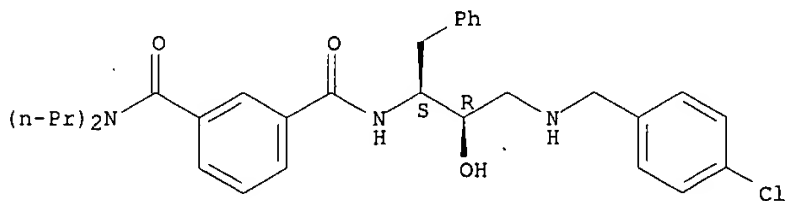
Absolute stereochemistry.



RN 388062-27-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[[4-chlorophenyl]methyl]amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

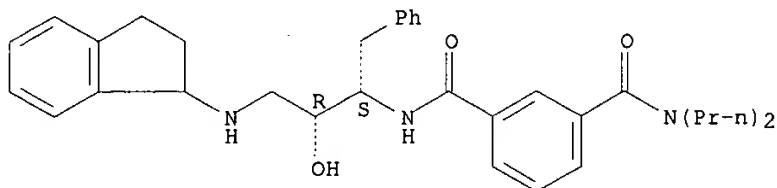


RN 388062-29-1 CAPLUS

09/288,556

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-[(2,3-dihydro-1H-inden-1-yl)amino]-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

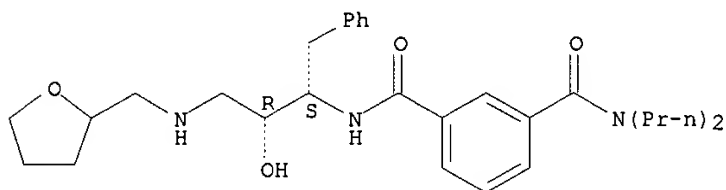
Absolute stereochemistry.



RN 388062-31-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[[tetrahydro-2-furanyl)methyl]amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

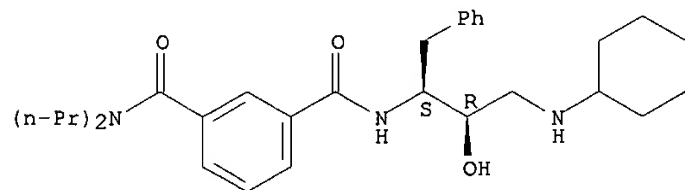
Absolute stereochemistry.



RN 388062-34-8 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-3-(cyclohexylamino)-2-hydroxy-1-(phenylmethyl)propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

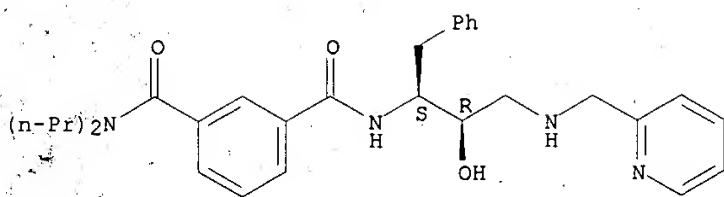


RN 388062-35-9 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-2-hydroxy-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

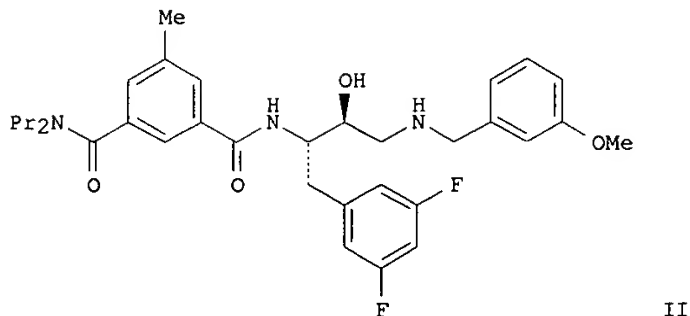
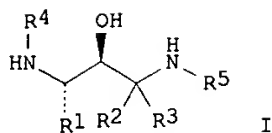
09/288,556



L6 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:31396 CAPLUS  
 DOCUMENT NUMBER: 136:102189  
 TITLE: Preparation of substituted amines for treating  
 Alzheimer's disease  
 INVENTOR(S): Fang, Lawrence Y.; Hom, Roy; John, Varghese;  
 Maillaird, Michel  
 PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 136 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002505	A2	20020110	WO 2001-US20852	20010629
WO 2002002505	A3	20020801		
WO 2002002505	C1	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FR, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002016320 A1 20020207 US 2001-896874 20010629 EP 1299349 A2 20030409 EP 2001-950719 20010629 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR US 2003096864 A1 20030522 US 2001-895871 20010629 JP 2004502664 T2 20040129 JP 2002-507762 20010629 PRIORITY APPLN. INFO.: US 2000-215323P P 20000630 WO 2001-US20852 W 20010629 OTHER SOURCE(S): MARPAT 136:102189 GI				



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl; R3 = H, (un)substituted alkyl; or R2 and R3 are taken together with the carbon to which they are attached to form (un)substituted 3-7 membered carbo(or hetero)cycle; R4 = RX; X = CO, SO<sub>2</sub>; R = Ph, naphthyl, indanyl, etc.; R5 = alkyl, (CH<sub>2</sub>)<sub>0-3</sub>cycloalkyl, etc.], useful as  $\beta$ -secretase inhibitors, were prepared Thus, reacting (2S,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with N,N-dipropylamidoisophthalic acid in the presence of Et<sub>3</sub>N, HOBT and EDC in CH<sub>2</sub>Cl<sub>2</sub> afforded (1S,2S)-II.

IT **388077-90-5P 388077-92-7P**

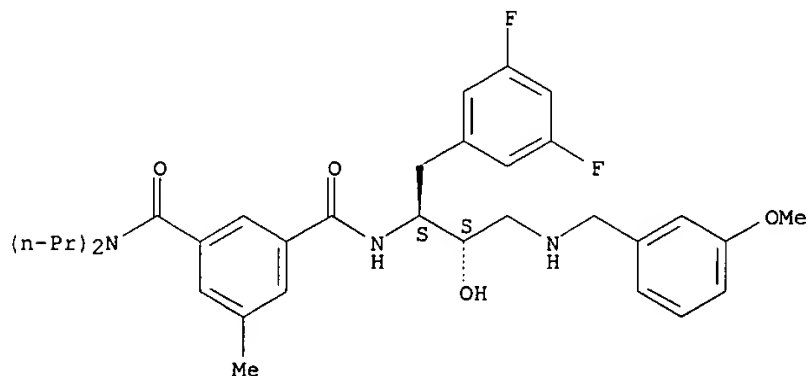
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted amines for treating Alzheimer's disease)

RN 388077-90-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N'-[(1S,2S)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[[[(3-methoxyphenyl)methyl]amino]propyl]-5-methyl-N,N-dipropyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

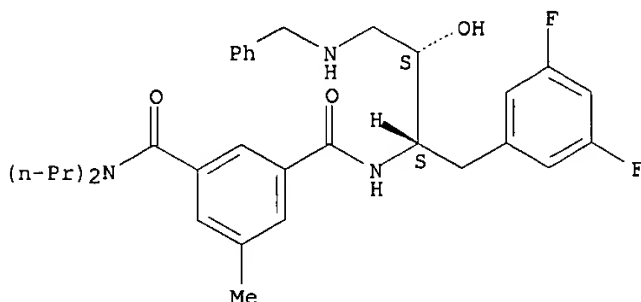




09/288,556

RN 388077-92-7 CAPLUS  
CN 1,3-Benzenedicarboxamide, N'-[(1S,2S)-1-[(3,5-difluorophenyl)methyl]-2-hydroxy-3-[(phenylmethyl)amino]propyl]-5-methyl-N,N-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



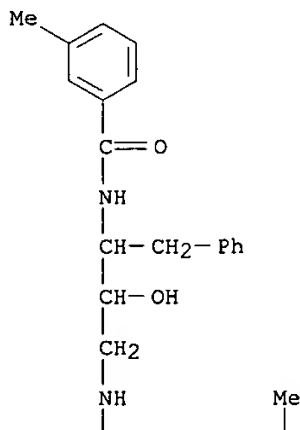
L6 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1996:506087 CAPLUS  
DOCUMENT NUMBER: 125:168656  
TITLE: HIV protease inhibitors  
INVENTOR(S): Abbenante, John; Bergman, Doug; Brinkworth, Ross;  
Dancer, Robert; Garnham, Bronwyn; Hunt, Peter;  
Fairlie, David; March, Darren; Martin, Jennifer; Reid,  
Robert  
PATENT ASSIGNEE(S): University of Queensland, Australia  
SOURCE: PCT Int. Appl., 84 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9616950	A1	19960606	WO 1995-AU817	19951204
W:	AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9641118	A1	19960619	AU 1996-41118	19951204
US 6043357	A	20000328	US 1997-849599	19970909
PRIORITY APPLN. INFO.:			AU 1994-9825	19941202
			WO 1995-AU817	19951204
OTHER SOURCE(S):		MARPAT 125:168656		
GI				

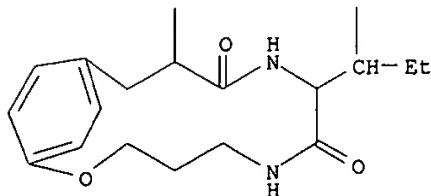
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

- AB HIV-1 protease inhibitors which include an N-terminal ring I or a C-terminal ring II or both rings I and II [R = Asn, Ile, Val, or Glu side chain, C1-C6 alkyl, cycloalkyl; X = (CH<sub>2</sub>)<sub>n</sub> (n = 3-6), CH(OH)CH(OH)CH<sub>2</sub>, CH(CO<sub>2</sub>H)CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>CONHCHR<sub>1</sub>, where R<sub>1</sub> = D- or L-amino acid, C1-C6 alkyl] were prepared. Thus, cyclic peptide III (R and S isomers) was prepared via O-alkylation of Boc-Tyr-OH, conversion to the tyrosylmethyl bromide derivative, coupling with resin-bound H-Pro-Ile-Val-NH<sub>2</sub>, etc. HIV-1 protease inhibitory data 134 are tabulated for 134 synthesized cyclic peptides.
- IT **175170-13-5**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (preparation of cyclic peptides as HIV protease inhibitors)
- RN 175170-13-5 CAPLUS
- CN Benzamide, N-[2-hydroxy-3-[[8-(1-methylpropyl)-7,10-dioxo-2-oxa-6,9-diazabicyclo[11.2.2]heptadeca-13,15,16-trien-11-yl]amino]-1-(phenylmethyl)propyl]-3-methyl- (9CI) (CA INDEX NAME)

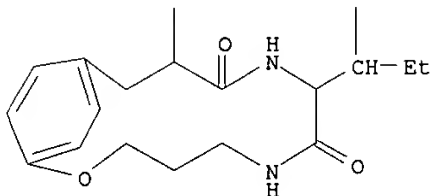
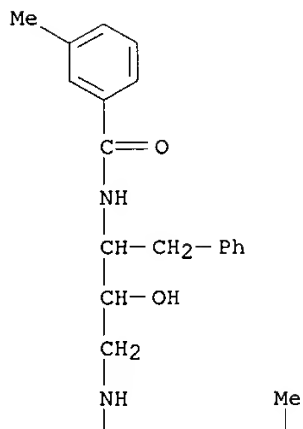
PAGE 1-A



PAGE 2-A



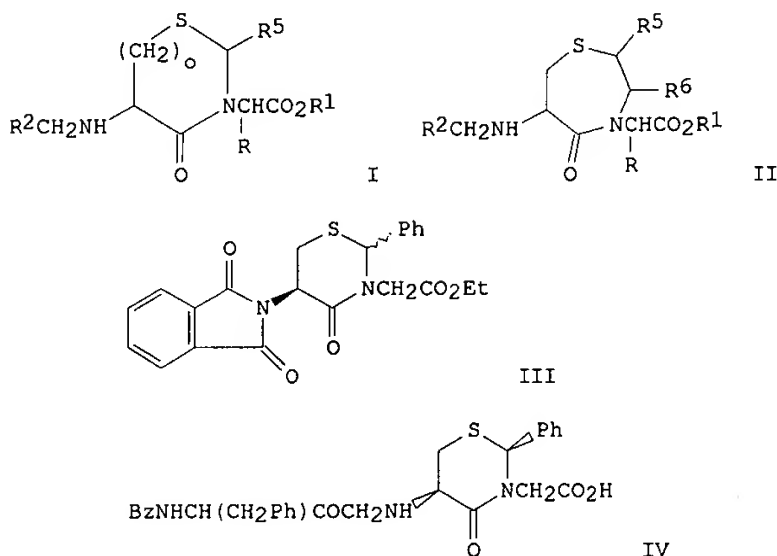
ACCESSION NUMBER: 1996:172301 CAPLUS  
DOCUMENT NUMBER: 124:249757  
TITLE: Substrate-based cyclic peptidomimetics of Phe-Ile-Val that inhibit HIV-1 protease using a novel enzyme-binding mode  
AUTHOR(S): March, Darren R.; Abbenante, Giovanni; Bergman, Douglas A.; Brinkworth, Ross I.; Wickramasinghe, Wasantha; Begun, Jake; Martin, Jennifer L.; Fairlie, David P.  
CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, 4072, Australia  
SOURCE: Journal of the American Chemical Society (1996), 118(14), 3375-9  
CODEN: JACSAT; ISSN: 0002-7863  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Results are presented for inhibitors of HIV-1 protease that demonstrate a new strategy for developing peptidomimetics, involving the replacement of flexible segments of peptide substrates with conformationally constrained hydrolytically-stable macrocyclic structural mimics. A 15-membered macrocycle that imitates the tripeptide Phe-Ile-Val was designed and incorporated into the C-terminus of Ac-Leu-Val-Phe-CHOHCH<sub>2</sub>-(Phe-Ile-Val)-NH<sub>2</sub>, an inhibitor of HIV-1 protease derived from a substrate sequence. Advantages of the macrocycle over the acyclic peptide include constraining its components into their bioactive conformation and protecting the amide bonds from enzymic degradation, the cycle being stable to acid, gastric proteases, and plasma. Mol. modeling and X-ray structural studies reveal that the cyclic inhibitors have a unique enzyme-binding mode, the sterically unencumbered hydroxyethylamine isostere binds via both its hydroxyl and protonated nitrogen to the anionic Asp25 catalytic residues. The novel macrocycle superimposes well on the linear peptidic inhibitor for which it was designed as a structural mimic. Structural mimicry led to functional mimicry as shown by comparable inhibition of the protease by cyclic and acyclic mols. Further modification of the acyclic N-terminus (Leu-Val-Phe) gave stable, water-soluble, potent inhibitors of HIV-1 protease. This approach may have general application to the development of mimetics of other bioactive peptides, including inhibitors of other enzymes.  
IT 175170-13-5P  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(cyclic peptidomimetics as HIV-1 protease inhibitor; substrate-based cyclic peptidomimetics of Phe-Ile-Val that inhibit HIV-1 protease using a novel enzyme-binding mode)  
RN 175170-13-5 CAPLUS  
CN Benzamide, N-[2-hydroxy-3-[[8-(1-methylpropyl)-7,10-dioxo-2-oxa-6,9-diazabicyclo[11.2.2]heptadeca-13,15,16-trien-11-yl]amino]-1-(phenylmethyl)propyl]-3-methyl- (9CI) (CA INDEX NAME)



L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1985:471331 CAPLUS  
 DOCUMENT NUMBER: 103:71331  
 TITLE: Acylamino oxo or hydroxy-substituted alkylamino  
 thiazines and thiazepines  
 INVENTOR(S): Weller, Harold N., III; Gordon, Eric M.; Karanewsky,  
 Donald S.; Ryono, Denis E.  
 PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA  
 SOURCE: U.S., 16 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4512988	A	19850423	US 1984-585058	19840301
AU 8539255	A1	19850912	AU 1985-39255	19850228

AU 577831	B2	19881006		
EP 154904	A1	19850918	EP 1985-102280	19850228
EP 154904	B1	19871028		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8501555	A	19851030	ZA 1985-1555	19850228
AT 30429	E	19871115	AT 1985-102280	19850228
CA 1242438	A1	19880927	CA 1985-475365	19850228
JP 60202870	A2	19851014	JP 1985-41770	19850301
JP 06088989	B4	19941109		
PRIORITY APPLN. INFO.:			US 1984-585058	19840301
			EP 1985-102280	19850228
OTHER SOURCE(S):			CASREACT 103:71331	
GI				



AB Antihypertensive (no data) thiazines and thiazepines I and II [R = H, alkyl, aminoalkyl, hydroxyalkyl, haloalkyl; R1 = H, alkyl, PhCH2, Ph2CH, Me3SiCH2CH2, salt forming ion, CHR7O2CR8 (R7 = H, alkyl, cycloalkyl, Ph; R8 = R7, alkoxy, PhCH2, PhCH2CH2); R2 = R3(CH2)mCONHCH[(CH2)nR4]C(Z); R3 = (substituted) Ph, thienyl, furyl, pyridyl; R4 = R3, OH, NH2, SH, halo, indolyl, imidazolyl, alkylthio, guanidino, carbamoyl, cycloalkyl; m = 0-4; n = 1-4; Z = O, (H, OH); R5, R6 = H, alkyl, cycloalkylalkyl, R5R6 = benzo; o = 1, 2] were prepared via inter- and intramol. cyclocondensations of cysteine derivs. Thus, cyclocondensation of N-phthaloyl-L-cysteine with PhCH:NCH2CO2Et gave thiazineacetate III as a mixture of diastereomers, the (2S)-isomer of which was transesterified with Me3SiCH2CH2OH, deprotected, alkylated with (S)-PhCH2CH(NHBz)COCH2Cl and hydrolyzed to give [2S-[2 $\alpha$ ,5 $\alpha$ (S)]]-thiazine IV.

IT 97246-59-8P 97549-62-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 97246-59-8 CAPLUS

CN 2H-1,3-Thiazine-3(4H)-acetic acid, 5-[[3-(benzoylamino)-2-hydroxy-4-

PRIORITY APPLN. INFO.:

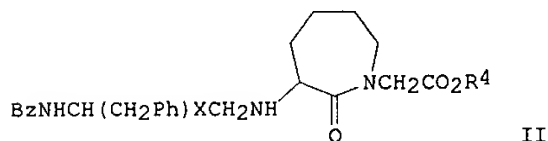
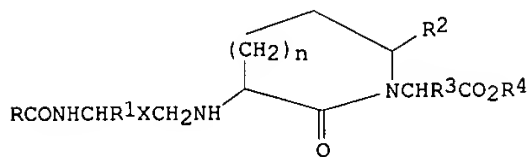
US 1983-549931

19831109

OTHER SOURCE(S):

CASREACT 102:78746

GI



AB Antihypertensive (no data) lactams I [ $n = 1-4$ ;  $X = \text{CO}, \text{CHOH}$ ;  $R = R_5$ ;  $R_1 = \text{H}, \text{alkyl}, R_5, \text{cycloalkyl}, \text{cycloalkylalkyl}, 3\text{-indolyl}, 3\text{-indolylalkyl}, \text{hydroxyalkyl}, \text{imidazolylalkyl}, \text{aminoalkyl}, \text{mercaptoalkyl}, \text{alkylthioalkyl}, \text{guanidinoalkyl}, \text{carbamoylalkyl}$ ;  $R_2 = \text{H}, \text{alkyl}, \text{cycloalkyl}, \text{cycloalkylalkyl}, R_5$ ,  $R_3 = \text{H}, \text{alkyl}, \text{aminoalkyl}, \text{hydroxyalkyl}, \text{haloalkyl}$ ;  $R_4 = \text{H}, \text{alkyl}, \text{CH}_2\text{Ph}, \text{CHPh}_2, 1\text{-acyloxyalkyl}, \text{cation}$ ;  $R_5 = (\text{un})\text{substituted Ph}, \text{phenylalkyl}, \text{thienyl}, \text{thienylalkyl}, \text{furyl}, \text{furylalkyl}, \text{pyridyl}, \text{pyridylalkyl}$ ] were prepared. Thus, (S)-II ( $R_4 = \text{H}, X = \text{CO}$ ) was prepared from  $\text{Me}_3\text{CO}_2\text{C-Lys}(\text{CO}_2\text{CH}_2\text{Ph})\text{-OH}$  and (S)- $\text{BzNHCH}(\text{CH}_2\text{Ph})\text{COCH}_2\text{Cl}$  in 6 steps. II ( $R_4 = \text{CH}_2\text{Ph}, X = \text{CO}$ ) was reduced with  $\text{NaBH}_4$  and hydrogenolyzed over  $\text{Pd-C}$  to give II ( $R_4 = \text{H}, X = \text{CHOH}$ ).

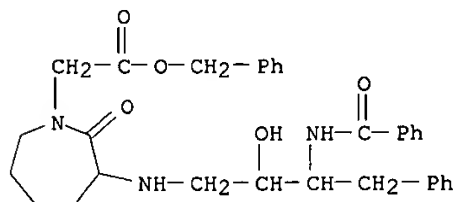
IT 93960-65-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenolysis of)

RN 93960-65-7 CAPLUS

CN 1H-Azepine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)



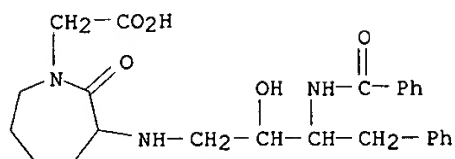
IT 93960-66-8P 93960-67-9P 93960-71-5P

93960-72-6P 93960-73-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

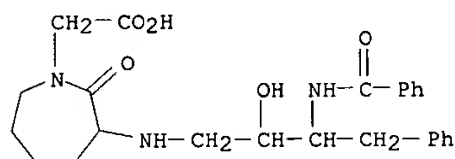
RN 93960-66-8 CAPLUS

CN 1H-Azepine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo- (9CI) (CA INDEX NAME)



RN 93960-67-9 CAPLUS

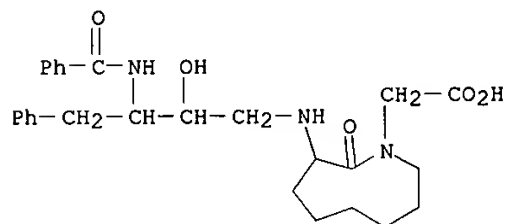
CN 1H-Azepine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

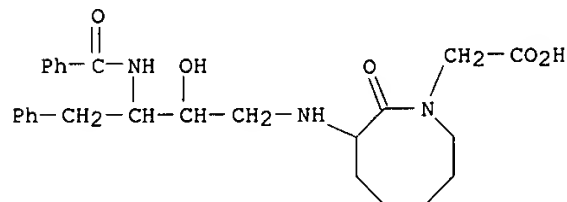
RN 93960-71-5 CAPLUS

CN 1H-Azonine-1-acetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]octahydro-2-oxo- (9CI) (CA INDEX NAME)



RN 93960-72-6 CAPLUS

CN 1(2H)-Azocineacetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-phenylbutyl]amino]hexahydro-2-oxo- (9CI) (CA INDEX NAME)

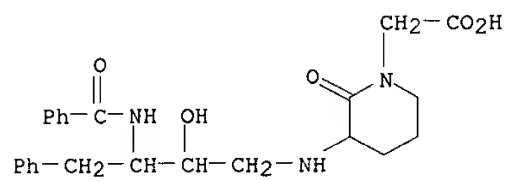


RN 93960-73-7 CAPLUS

CN 1-Piperidineacetic acid, 3-[[3-(benzoylamino)-2-hydroxy-4-

09/288,556

phenylbutyl]amino]-2-oxo- (9CI) (CA INDEX NAME)



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